Dissertation on

"BACTERIAL ETIOLOGICAL AGENTS RESPONSIBLE FOR SEPSIS IN CHILDREN AGED 1-36 MONTHS AND SUSCEPTIBILITY PATTERNS OF ISOLATES"

Submitted in partial fulfillment of requirements of

M.D. PAEDIATRICS
BRANCH - VII

INSTITUTE OF CHILD HEALTH &HOSPITAL FOR CHILDREN

MADRAS MEDICAL COLLEGE

CHENNAI- 600 003

THE TAMILNADU
DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI

APRIL 2015

CERTIFICATE

This is to certify that the dissertation entitled **"BACTERIAL ETIOLOGICAL AGENTS RESPONSIBLE FOR SEPSIS IN CHILDREN AGED 1-36 MONTHS AND SUSCEPTIBILITY PATTERNS OF ISOLATES"** *i*s a bonafide work done by **DR.L.AJEITHA** at Madras Medical College, Chennai in partial fulfillment of the university rules and regulations for award of M.D., Degree in Pediatrics (BRANCH VII) during the academic year 2012-2015.

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DECLARATION

I solemnly declare that this dissertation entitled **"BACTERIAL ETIOLOGICAL AGENTS RESPONSIBLE FOR SEPSIS IN CHILDREN AGED 1-36 MONTHS AND SUSCEPTIBILITY PATTERNS OF ISOLATES"** was done by me at Madras Medical College and Institute of Child Health and Hospital for Children, during 2012-2015 under the guidance and supervision of **DR. ANNAMALAI VIJAYARAGHAVAN M.D., DCh.,** and **DR.N.DEVASENA M.D.** This dissertation is submitted to **The Tamilnadu Dr.M.G.R Medical University** towards the partial fulfillment of requirements for the award of **M.D Degree in Pediatrics (Branch – VII)**

Place: Chennai **Signature of the Candidate**

SPECIAL ACKNOWLEGEMENT

My sincere thanks to **Prof.R.VIMALA M.D.,** The Dean, Madras Medical College, for allowing me to do this dissertation and utilize the Institutional facilities.

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to the Director and Superintendent of ICH & HC **Prof S.SUNDARI M.D., DCH.,** for permitting me to carry out this study.

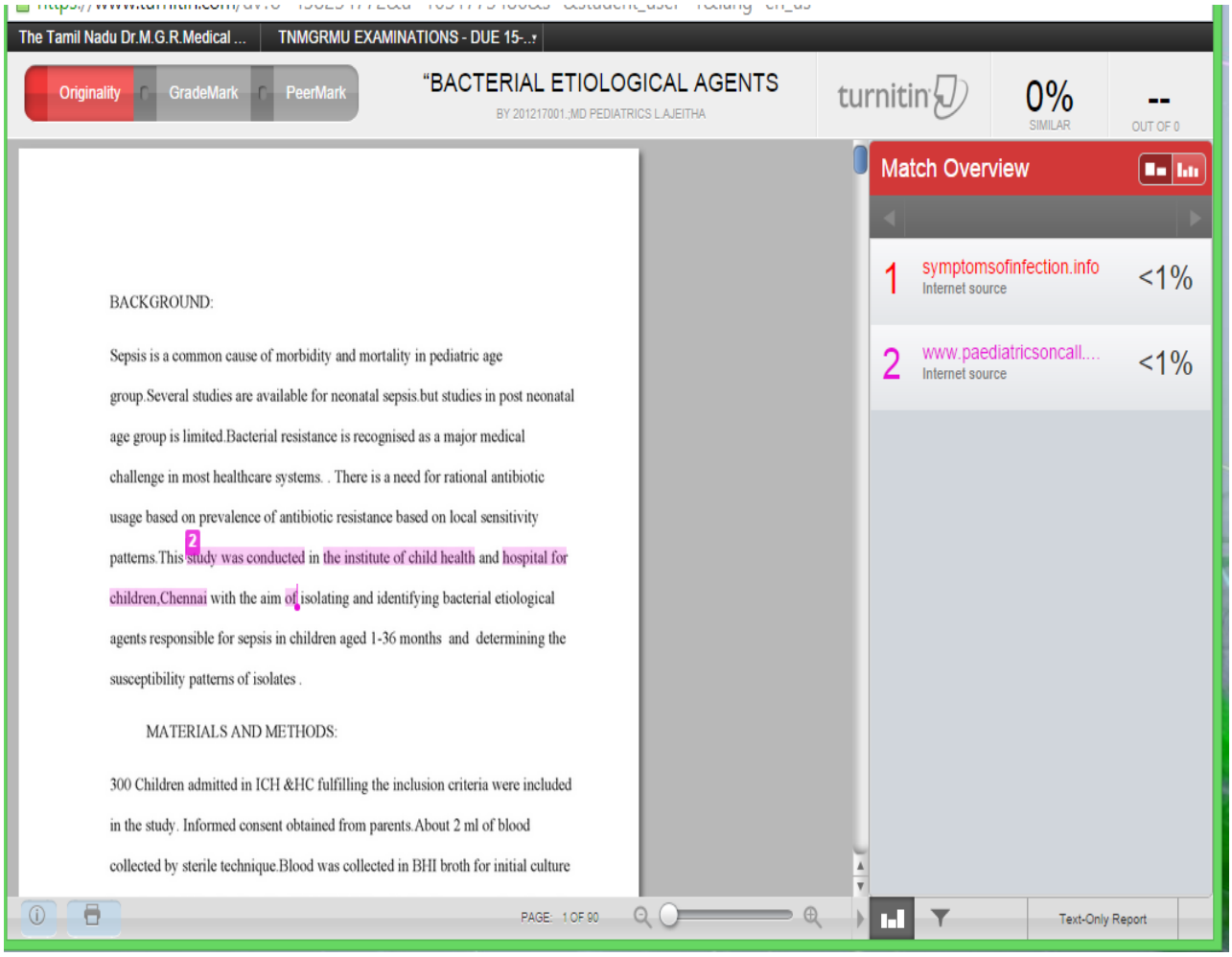
I am deeply indebted to so many for guiding and helping me in my endeavor in making this dissertation a reality. I express my deep sense of gratitude to my respected teacher and guide, **PROF.ANNAMALAI VIJAYARAGHAVAN,** Professor of Pediatrics, Institute of child health and hospital for children,chennai, for his valuable guidance and constant encouragement throughout the course and the present study.

I express my heartfelt thanks to **Dr.N.DEVASENA,** Professor of Microbiology, Institute of child health and hospital for children,chennai for her timely advice guidance and encouragement at every stage in the conduct of this study.

I would like to thank **DR.SRINIVASAN .S**, Registrar, for his valuable suggestion and guidance in doing this project.

My sincere gratitude to **DR.K.NEDUNCHELIAN, DR.N.BALAKRISHNAN, DR.M.S.MANI, DR.PERUMAL PILLAI, DR.S.BHARATHI, DR.SURESH** and all my teachers of for their constant support of valuable suggestions at every stage of this study. My colleagues and fellow have been the source and support of companionship throughout this course and I am indebted to them.

I thank my father DR.M.LOGANATHAN who helped me with all the statistical analysis,my mother DR.V.THAMILSELVI and my husband DR.ARULMURUGAN.R without whose constant support and love nothing would have been possible. I am grateful to the patients for their co-operation in this study. I will be failing in duty, if I do not express my gratitude to all the patients, who were the subjects of this study. My sincere thanks to them for being my study subjects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BACKGROUND:
Sepsis is a common cause of morbidity and mortality in pediatric age group.Several studies are available for neonatal sepsis.but studies in post neonatal age group is limited.Bacterial resistance is recognised as a major medical challenge in most healthcare systems. . There is a need for rational antibiotic usage based on prevalence of antibiotic resistance based on local sensitivity patterns.This study was conducted in the institute of child health and hospital for children,Chennai with the aim of isolating and identifying bacterial etiological agents responsible for sepsis in children aged 1-36 months and determining the susceptibility patterns of isolates .
MATERIALS AND METHODS:
300 Children admitted in ICH &HC fulfilling the inclusion criteria were included in the study. Informed consent obtained from parents.About 2 ml of blood collected by sterile technique.Blood was collected in BHI broth for initial culture
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CERTIFICATE OF APPROVAL

To
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Post Graduate in MD Paediatrics,
Institute of Child Health,
Madras Medical College,
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Dear Dr. L. Ajeitha,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Bacterial etiological agents responsible for sepsis in children aged 1-36 months and their antibiotic susceptibility patterns"** No.17042014

The following members of Ethics Committee were present in the meeting held on 08.04.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C. Rajendran, M.D.	-- Chairperson
2.	Prof. Kalaiselvi, MD Vice-Principal, MMC, Ch-3	-- Member Secretary
3.	Prof. Nandhini, M.D. Inst. of Pharmacology, MMC, Ch-3.	-- Member
4.	Prof. Bhavani Shankar, M.S. Prof & HOD of General Surgery, MMC, Ch-3.	-- Member
5.	Prof. V. Padmavathi, M.D. I/c Directory of Pathology, MMC, Ch-3.	-- Member
6.	Thiru. S. Govindasamy, BA., BL	-- Lawyer
7.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist
8.	Thiru. S.Rameshkumar Administrative Officer, MMC, Ch-3.	-- Lay Person

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

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BACKGROUND:

Sepsis is a common cause of morbidity and mortality in pediatric age group.Several studies are available for neonatal sepsis.but studies in post neonatal age group is limited.Bacterial resistance is recognised as a major medical challenge in most healthcare systems. . There is a need for rational antibiotic usage based on prevalence of antibiotic resistance based on local sensitivity patterns.This study was conducted in the institute of child health and hospital for children,Chennai with the aim of isolating and identifying bacterial etiological agents responsible for sepsis in children aged 1-36 months and determining the susceptibility patterns of isolates .

MATERIALS AND METHODS:

300 Children admitted in ICH &HC fulfilling the inclusion criteria were included in the study. Informed consent obtained from parents.About 2 ml of blood collected by sterile technique.Blood was collected in BHI broth for initial culture by automated blood culture(bacT/ALERT PF) and subcultures were done based on isolates.Antibiotic susceptibility of the isolates were

determined by Kirby-Baeur disc diffusion method.Primary outcomes of the study were bacteriae isolated and their antibiotic susceptibility pattern.The secondary outcome studied was their antibiotic resistance (ESBL,MRSA,Metallo betalactamases)

RESULTS:

The percentage of culture positivity was 27%(80/300).Staphlococcus aureus was the most common organism isolated accounting for 58.75% of overall isolates.The next most common being klebsiella.(15%)The percentage of MRSA of the Staph isolates was 39.1%.The percentage of VRSA was 17.3%.Among klebsiella ESBL production was 16.67% and all were sensitive to meropenam.Enterococci showed high degree of resistance to cephalosporins(61.6%).VRE(Vancomycin resistant enterococci) acoounted for 16.67%. Among all isolates ,the antibiotic with maximum coverage was amikacin followed by ciprofloxacin.Th overall duration of stay was 11.65 days.The mortality rate among culture positive patients and culture negative patients were 8.75% and 2.7% respectively.Serum procalcitonin levels were found to be significantly raised ($P<0.01$) in culture positive patients when compared to culture negative cases.

INTERPRETATION AND CONCLUSIONS:

There is an shift of organisms grown from the gram negative to gram positive spectrum,with the most common organism being Staphlycoccus aureus. None of the isolates were H.Influenza meaning increasing immunization coverage(74%) against them decreasing their incidence.

The prevalence of MRSA is high(39%).There is also increasing resistance to b-lactam antibiotics among all gram positive isolates and ESBL production among kelbsiella.This increases the hospital stay and more monetary wastage for the higher antibiotics used and higher toxicity.

Key words: Bacteremia; Extended-spectrum beta lactamases (ESBLs); Klebsiella; Methicillin resistant Staphylococcus aureus (MRSA); Staphylococcus aureus

INTRODUCTION:

Sepsis is defined as host response to infection and is an important cause of morbidity and mortality all over the world. The Surviving Sepsis Campaign pointed out sepsis as a fundamental challenge(1).

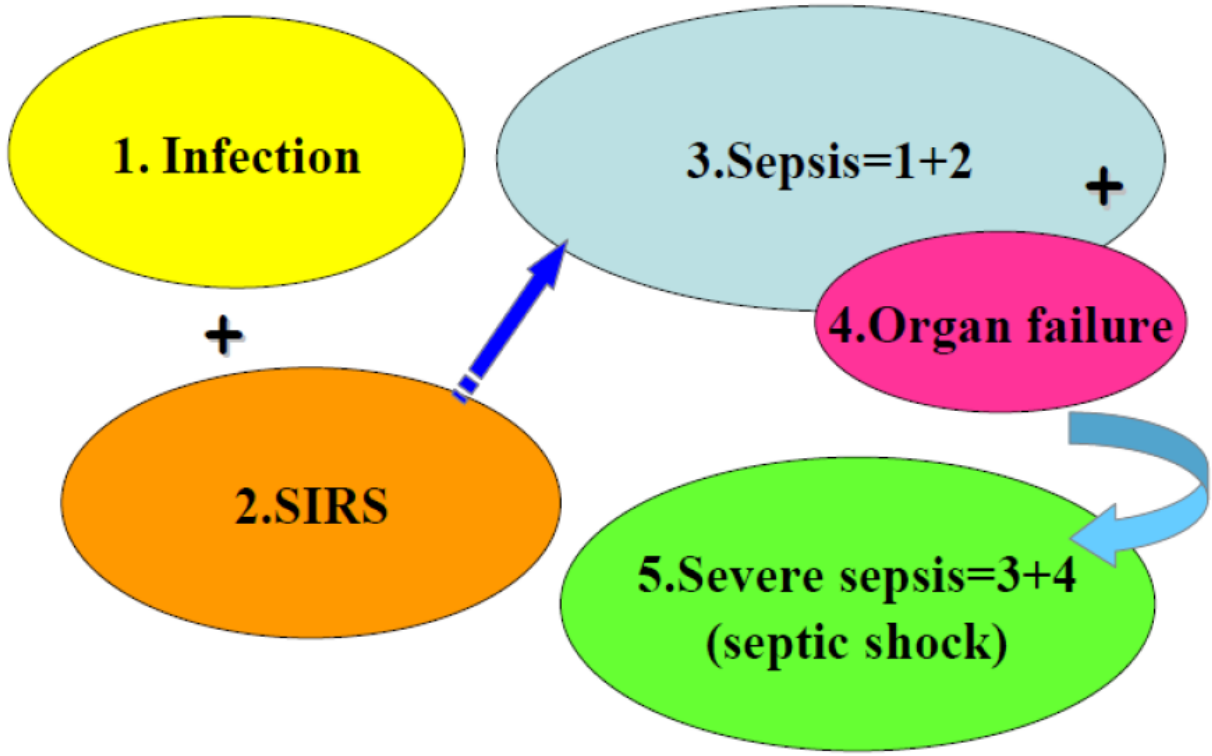
The increasing incidence of sepsis may be linked to chronic diseases, indwelling catheters, misuse of antimicrobials and mechanical devices(2).

Antibiotic therapy in infants and children presents many challenges.There are differences among age groups with respect to pathogenic groups responsible for infections in the particular age group and also local prevalence and susceptibility patterns.

The wide complexity of organisms necessitates knowledge of local susceptibility.

This study is an attempt to find the bacteria involved in sepsis and their antibiotic susceptibility in ICH & HC,Chennai

Sepsis is defined as **SIRS** resulting from a suspected or proven infectious etiology. (3)The clinical spectrum of sepsis begins when a systemic (e.g., bacteremia, rickettsial disease, fungemia, viremia) or localized (e.g., meningitis, pneumonia, pyelonephritis) infection progresses from sepsis to **severe sepsis** (the presence of sepsis combined with organ dysfunction). Further deterioration leads to **septic shock** (severe sepsis plus the persistence of hypoperfusion or hypotension despite adequate fluid resuscitation or a requirement for vasoactive agents)(3), **MODS**, and possibly death . This is a complex spectrum of clinical problems that is a leading cause of mortality in children worldwide. Outcomes improve with early recognition and treatment.



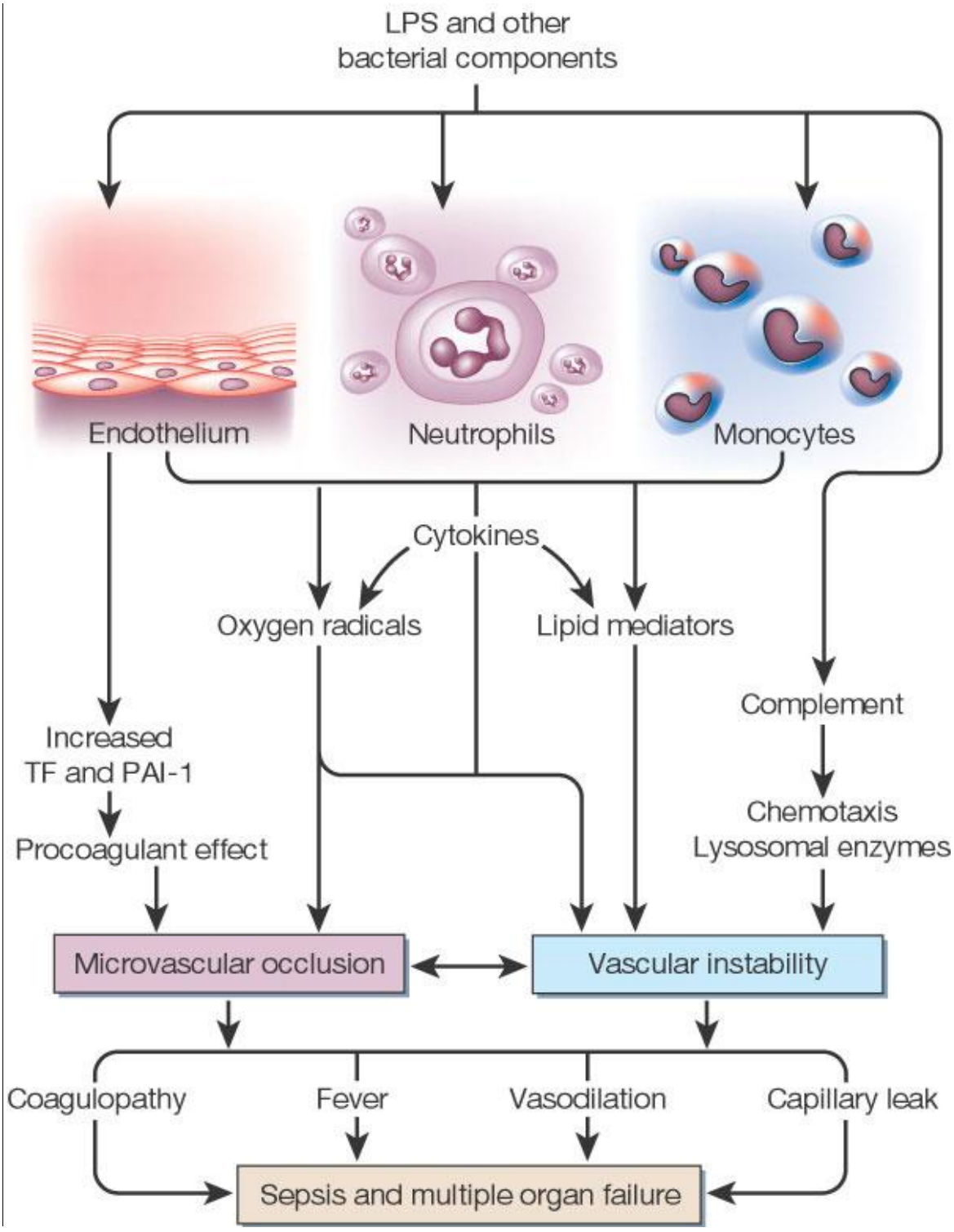
PATHOPHISIOLOGY OF SEPSIS

The word sepsis is derived from the Greek word ‘septikos’, meaning ‘rotten’ or “to make putrid”. Sepsis is defined as systemic host response to microbes in previously sterile tissue. In its severe form, it is characterized by multitude of end-organ dysfunction often away from the prime site of infection. The pathophysiology of sepsis is a continuum. The normal response to infection is both to identify pathogen invasion and to initiate tissue repair. The immune response comprises responses by innate immunity and adaptive immunity. The innate immunity response forms front-line reaction against invading pathogens. It consists of recognition of components of microbes, activation of phagocytosis (e.g. neutrophils, monocytes, eosinophils, and macrophages), coagulation, complement system and production of acute phase proteins.Adaptive immunity consists of responses by cell-mediated and humoral immunity.

These phenomena function in parallel and are contingent on each other. Both these give rise to proinflammatory and anti-inflammatory responses. If this process is disturbed, a sequence of events take place in which promotion and liberation of inflammatory mediators inevitably leads to sepsis.(4)

Innate immune response

The physical barriers to host invasion are externally formed by skin and internally formed by mucous membranes lining the gastrointestinal, respiratory and genitourinary tracts. They form a mechanical barrier against invading pathogens in assosiation with the normal local flora. In hospital environment patient's intravenous cannulas, indwelling catheters and urinary catheters are considered as possible sources of infection(5).Sepsis may be due to numerous invasive pathogens including bacteria, viruses, fungi and parasites. The structural components of a microbe responsible for initiating the septic process are important for understanding the mechanisms of inflammation and also for identifying potential therapeutic targets. Endotoxin is a lipopolysaccharide located in the outer portion of cell membrane of gram-negative bacteria. Exposure to exotoxins produced by gram positive bacteria ,endotoxins or any other types of microbial components initiates intracellular events in epithelium ,endothelium, immune cells and neuroendocrine system through microbe associated molecular patterns(6)

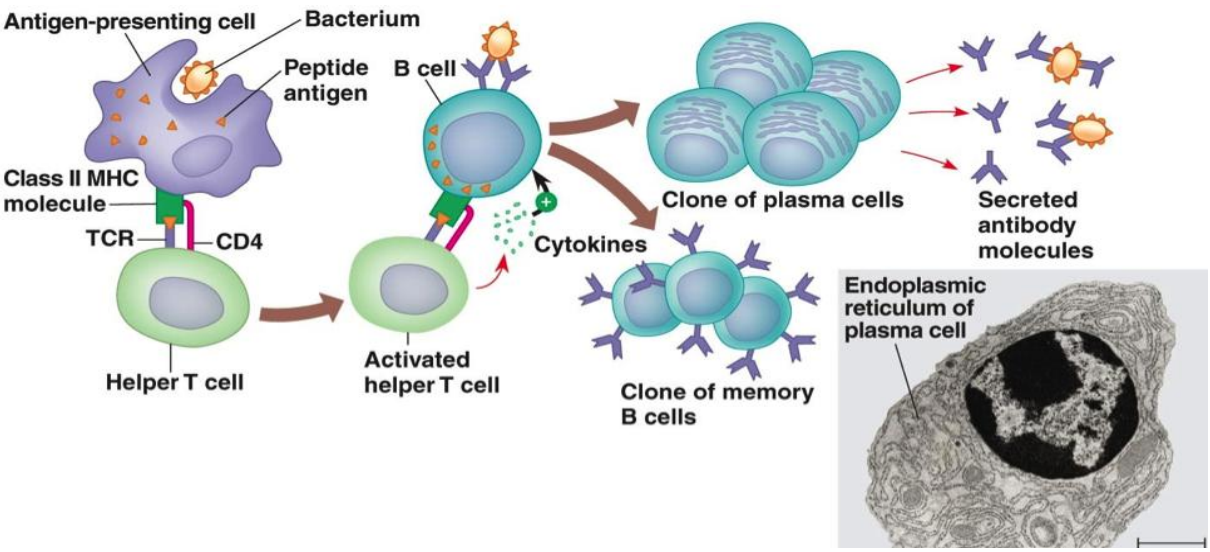


The initiation of response involves pattern recognition receptors which recognize specific microbial structures(7). Parts of this are toll-like receptors

(TLRs)- transmembrane proteins on the immune cell surfaces. They are capable of identifying the invading microbes. Microbes have unique cell wall molecules called pathogen-associated molecular patterns (PAMPs). The PAMPs adhere to TLRs on surface of immune cells. The binding in turn initiates intracellular signaling pathways. As a result of this proinflammatory cytokines are released. Monocytes and macrophages also participate in secretion of proinflammatory cytokines. Endothelial cells and neutrophils are activated to produce adhesion molecules. These help to kill pathogens, but also damage the endothelium. Macrophages release VEGF-like molecules, which increase vessel permeability and proliferation, leading to coagulation and inflammatory processes.(8)

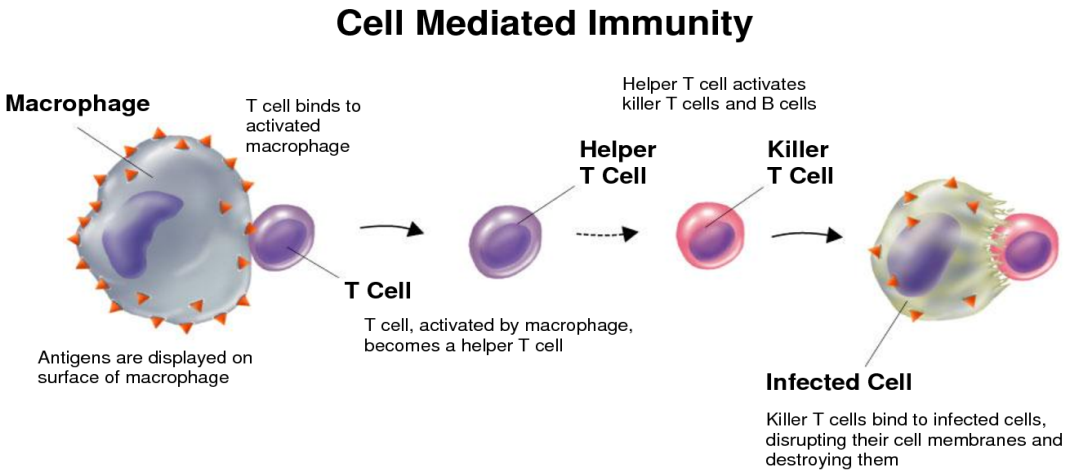
Adaptive immune response

Following the initial host-microbe interaction there is activation of adaptive immune response. This coordinates defense responses combining both cellular and humoral immune systems. Humoral immune response is mediated by antibodies (immunoglobulins) produced in B lymphocyte lineage cells (plasma cells). These secreted antibodies bind to antigens present on the surface of invading microbes, targeting them for destruction by components of the innate immune system.



Microbes are destroyed by the phagocytic cells (e.g., macrophages, neutrophils, or natural killer cells)along with the help of complement system activation or recognition by antibodies.(9)

Cell mediated immunity is immune response mediated by T lymphocytes. It comprises activation of natural killer cells, macrophages, antigen-specific cytotoxic T lymphocytes and release of cytokines in response to an antigen.



Cytotoxic T-lymphocytes (CD8 destroy cells infected by viruses or cells containing intracellular bacteriae. Helper T cells (CD4) release cytokines by differentiating into type 1 helper T-cells (Th1) and type 2 T helper -cells (Th2) (or other subsets of T cells). Th1 secretes pro-inflammatory cytokines and Th2 secretes anti-inflammatory cytokines. Proinflammatory cytokines (e.g. interleukin-6 (IL-6) ,interleukin-1 (IL-1), and tumor necrosis factor-alpha (TNF-α) contribute to elimination of the invading pathogens and anti inflammatory mediators (e.g. interleukin-10 (IL-10) and interleukin-4 (IL-4)) to control this response.(10) The proinflammatory response leads ultimately to damage of host tissues, while the anti-inflammatory response leads to leukocyte reprogramming and changes the immune status. During this

sequence, circulatory abnormalities (e.g., peripheral vasodilatation, intravascular volume depletion and myocardial depression) lead to an imbalance between systemic oxygen demand and delivery.(11)

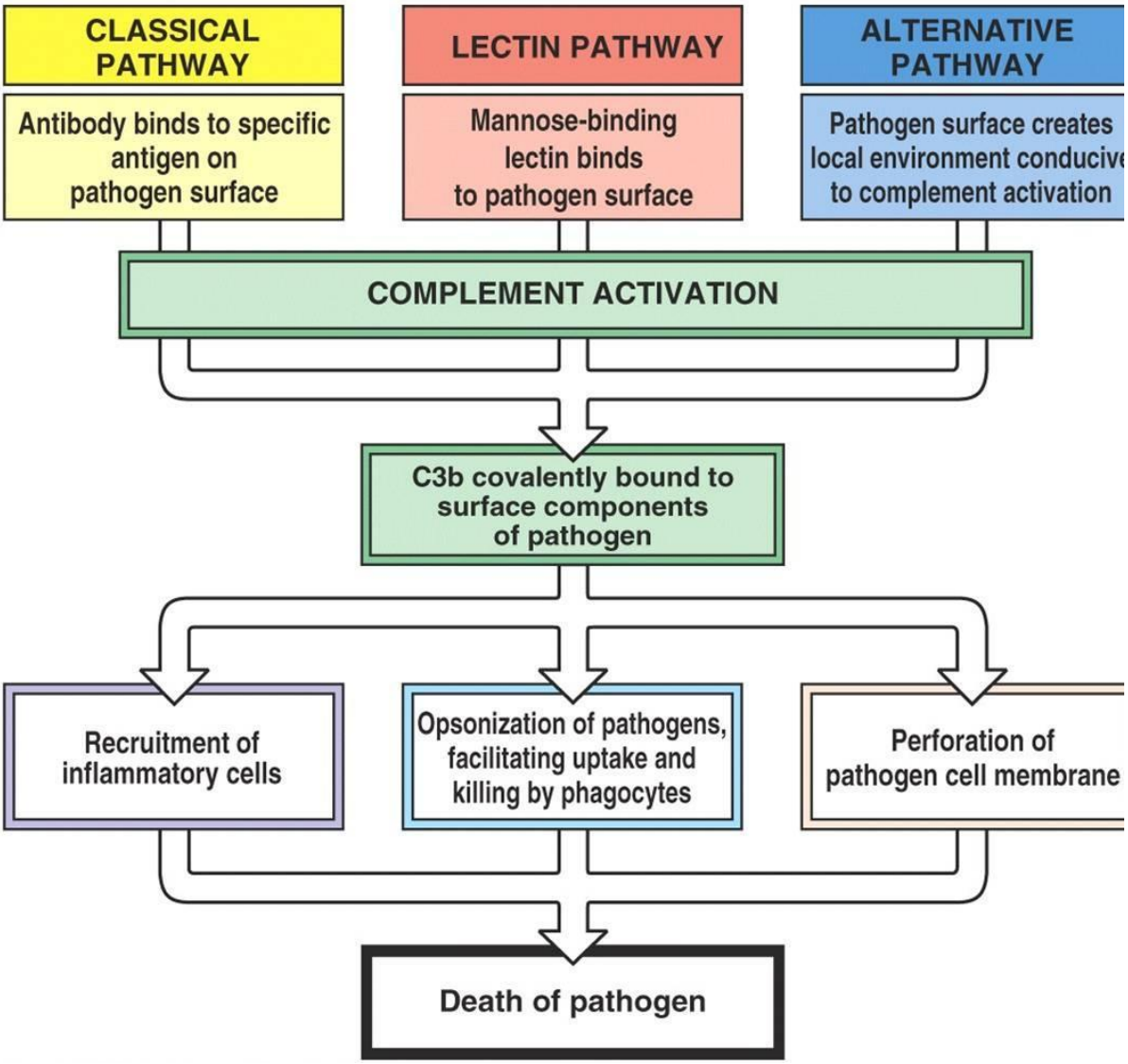
Complement system, coagulation and inflammation

The coagulation and complement system are major components of plasma cascades. These are closely related and activated in a contiguous manner by multiple common stimuli (e.g. infection, trauma).Both these contribute to inflammation and mutually interact at various stages.(12) Complement is a part of the innate immune system and also a mediator of antibody mediated immunity. Its major functions are defense against pyogenic bacterial infections ,linking innate and adaptive immunity and also clearance of immune complexes and other products of inflammatory response. Circulating components of complement system are activated by three pathways:

1.The classical pathway :Initiated by binding of component C1q to antigen antibody complex

2.The lectin pathway:Initiated by binding of mannose-binding lectin to the sugars present in bacterial cell wall

3.The alternative pathway: initiated after exposure to the surface molecules of invading pathogens.



After the end of these pathways various convertases (e.g. C3, C5) are released and these in turn facilitate phagocytosis of opsonised pathogens by neutrophils and macrophages, act as mediators of inflammation and participate in lysis of bacterial cell membrane. The regulatory mechanisms of complement system are balanced sensitively. The ultimate aim is to focus the activation of complement onto the surface of invading pathogens and at the same time limiting deposition on normal cells.(13) A very delicate balance of

pro-coagulant and anticoagulant factors maintains haemostasis.During normal conditions three anticoagulant pathways prevent widespread activation of coagulation:

1.antithrombin,

2. activated protein C

3. tissue factor pathway inhibitor.

During inflammation mediated activation of coagulation, all the three functions are impaired; IL-6 release initiates tissue factor upregulation, leading to coagulation cascade, whereas TNF-α mediates suppression of natural anticoagulants. This leads to Disseminated Intravascular Coagulation(DIC), which is thought to be pivotal in the pathogenesis of multiorgan dysfunction (MODS) in sepsis. Hence, sepsis is a chaotic environment with decreased anticoagulation, exacerbated coagulation and impaired fibrin removal.(14)

Coagulation and complement cascades are intended to act locally. In case they are activated systemically due to failure of relevant control mechanisms, the effect of this broad activation can be irrevocable.

Endothelium and inflammation

Vascular endothelial cells have an active role in regulation of blood vessel permeability, tone, coagulation, angiogenesis and leukocyte and platelet activation. Endothelial cells manufacture several pro- and anti-inflammatory molecules. They synthesize proteins which increase vascular permeability to large molecules (e.g. antibodies and complement components) and to fluid. (15) Various microbes adhere to the endothelium, leading to localized inflammation and recruitment of monocytes and neutrophils. Increase in vascular permeability leads to leukocyte migration into surrounding tissue in response to chemotactic factors created at the site of injury. Endotoxins or other foreign particles lead to neutrophil activation and also release of pro-inflammatory cytokines. This adhesion initiates the coagulation cascade.

Vascular endothelium is one of the main organs involved in pathogenesis of sepsis. Damage to endothelium may result in global tissue hypoxia or shock.(16) Increasing tissue hypoxia may finally lead to MODS and death.

MARKERS FOR SEVERE SEPSIS

In severe sepsis and other high grade infections, circulating levels of biomarkers depend on origin and extent of the infection.Also, microbes induce a distinct response in several organs, leading to variable diversity of biomarkers and mediators. It is obviously evident that any infection is too

complex to be confined to single cutoff of any biomarker. The dynamics of biomarker levels have prognostic significance and their increasing levels are found to be associated with unfavorable outcome and decreasing levels suggest favorable outcome.(17) Biomarkers are valuable and helpful tools in case of diagnostic dilemma of severe sepsis, especially in delineating severe sepsis from less severe forms of sepsis in very early phase of disease. Several treatment strategies are effective in sepsis, but the disease must be diagnosed early to be treated effectively.

Early diagnosis with unknown microbiological etiology, but early sepsis therapy is more effective than specific sepsis therapy initiated late. (18)This is true in neutropenic sepsis, where clinical findings and symptoms of infection may be obscure or absent. An ideal prognostic marker should distinguish septic infections from various other causes of systemic inflammatory response syndrome. The marker should also reflect the severity of infection and distinguish time periods with high risk of complications from periods with low risk.

Total leukocyte count and leukocyte differentiation are amongst the oldest markers of infection, but they are useless in patients with severe neutropenia. Procalcitonin(PCT) ,CRP and proinflammatory cytokines (IL-6 ,IL-8) are useful markers of inflammation. In addition to these markers, natriuretic

peptides, VEGF, lactate have been persistent interest of study. Various other potential future candidates are neopterin, lactoferrin and prostaglandins.(19)

C-reactive protein

CRP is a member of acute-phase reactants, because its levels rapidly rise in response to any inflammatory process. CRP is produced by hepatocytes, mainly under transcriptional control by IL-6. Around 90% of healthy population has CRP concentration < 3 mg/l. Synthesis after the initiating stimulus beginsrapidly and serum concentrations of CRP rise above 5 mg/l in about 6 hours.Peak values are achieved in about48 hours. The only determinant of circulating CRP concentration is its synthesis rate and it reflects the intensity of pathological process stimulating CRP production. (20) As soon as the stimulus terminates, circulating CRP falls rapidly.

Production of CRP is part of nonspecific acute-phase response to various forms of infection, inflammation and tissue damage. Persistent increase in CRP also occurs in chronic inflammatory disorders,which includes autoimmune diseases and malignancy. CRP has an important role in host defense by opsonization, complement action and inducing phagocytosis.(21) CRP is used clinically for monitoring autoimmune disorders and infections. CRP concentrations are clinically very useful when combined with a full

knowledge of all clinical and pathological results. Especially, in severe liver diseases CRP is formed at a markedly lower pace than in patients without liver disorders.(22)

The use of CRP is very common in several European countries mainly because of easy availability and its low costs in everyday clinical practice. In several studies, CRP has been used for comparison of other markers of inflammation, chiefly because of its well-known kinetics and its broad use in several infectious disease. The time taken from suspicion to diagnosis in sepsis is critical because in uncontrolled infections severe sepsis may occur rapidly, with a mortality of 20-52%. In recent sepsis studies, the slow kinetics of CRP initially has diminished its value as a very early marker of sepsis. The diagnostic use of CRP and various other inflammation markers was studied in patients with malignancy with suspected infection. Only procalcitonin was shown to be a good marker to differentiate bacteraemic patients and other patients.

CRP identifies a patient with infection, but whenever the time interval is short (<12 hours), the predictive capacity of CRP declines significantly. When kinetics of CRP during infections in leukemia patients were studied, it was evident that CRP over 100 mg/l predicted infection.(23) Another study evaluated the capacity of CRP and various other inflammatory markers to

predict bacteraemia in first 48 hours of fever in patients with neutropenia.(24) In initial 10 hours, CRP had a sensitivity of 42% and a specificity of 76% for bacteremia. Its positive predictive value was 33%. CRP reached its highest levels after 20 to 30 hours in febrile neutropenia in patients with bacteremia.

In another study there were no differences in early CRP concentrations between bacteraemic and non-bacteraemic patients.(25) The result was similar in the study of Sandri and colleagues(26), where PCT concentrations increased early only in bacteraemic patients with the highest levels at day 1 after the onset of fever. CRP reached its peak level also at day 1 after the onset of fever but could not distinguish bacteraemic patients from non-bacteraemic patients. Based on these studies, CRP is useless from a predictive point of view.

Vascular endothelial growth factor(VEGF)

Vascular endothelial growth factors (VEGF)is an important signaling protein involved in both angiogenesis (growth of blood vessels from already existing vasculature) and vasculogenesis (de novo formation of embryonic circulatory system).

VEGF is the most potent factor regulating microvascular permeability and angiogenesis. (27)VEGF production is increased in hypoxemic cells. Whenever a cell is deficient in O2, it synthesizes hypoxia-inducible factor (HIF). This in turn stimulates release of VEGF. The pivotal role of VEGF as a mediator of vascular permeability is important in various infections. VEGF is found to cause vasodilatation conditioned by endothelial nitric oxide synthase (eNOS) in patients with sepsis. (28)Two study groups have reported increase of VEGF levels in severe sepsis. Pickkers et al (29) have studied septic shock in meningococcal infections as the prototype of gram negative septic shock in children. Plasma concentrations of VEGF were measured in the first 48 hours and found to be highest in presence of septic shock. Concentrations of VEGF at admission correlated with the infection severity Van der Flier et al measured VEGF levels in patients having severe sepsis in ICU.(30) They have found that VEGF levels were elevated significantly in patients with severe sepsis when compared to healthy controls. Also, plasma VEGF levels in non-survivors were higher compared to survivors. Increased VEGF levels at the entry of study also correlated with the MODS severity during the course of the disease. Karlsson et al studied plasmaVEGF levels in ICU patients with severe sepsis to predict mortality and organ dysfunction. (31)They have found that VEGF levels were raised in patients with severe

sepsis when compared with controls. Low levels of circulating VEGF were found to be associated with renal and hematological dysfunction, suggesting probable disturbed VEGF production in severe sepsis. Further, very low VEGF concentrations were associated with mortality and very severe forms of organ dysfunction, possibly because of injury to endothelium.

Amino-terminal pro-brain natriuretic peptide

Brain natriuretic peptide (BNP) is a pro –hormone which is secreted by cardiomyocytes.BNP secretion is primarily a response to increased myocardial wall stress and it is aimed to sustain cardiovascular homeostasis by its natriuretic, vasodilatory and diuretic properties. (32)NT-pro BNP is an inactive metabolite of BNP. NT-proBNP has significantly longer plasma half-life and also better stability than BNP.This makes NT-pro BNP better applicable for clinical use. Increased in levels of both BNP and NT-pro BNP are recognized as early markers of both increased myocardial dysfunction and mortality in ICU setting.(33) Raised levels of natriuretic peptides are found to be markers of poor prognosis in patients with severe sepsis and septic shock.(34) Also patients with less severe infections seem to have raised levels of natriuretic peptides. A positive correlation between increased levels of BNP and IL-6 in patient having septic shock has been shown previously and in latest studies both BNP and NT-pro-BNP production are

linked to general inflammation. Rudiger et al have shown a correlation between NT-pro-BNP and also CRP levels in a group of haemodynamically unstable patients.Levels of NT-pro-BNP or BNP did not significantly differ between patients with septic shock and those with acute cardiac failure. (35)This result was similar to a study by Shor et al, where BNP levels positively correlated with CRP in septic patients without myocardial dysfunction.(36) Nevertheless, there was found to be a significant association between markedly elevated BNP values and both sepsis and 30-day mortality in patients . Nikolaou et al have shown that BNP levels were raised in acute phase of community-acquired infections without septic shock or severe sepsis. (37)

Other markers

Lactate

Lactate is a result of balance between lactate production and utilization. Hyperlactataemia is present typically in patients with septic shock or severe sepsis. In the above said patients both high lactate and poor lactate clearance have been recognized as early markers of mortality.(38) Hyperlactatemia can be secondary to anaerobic metabolism because of tissue hypoperfusion. The prognostic use of elevated serum lactate levels is well

established in patients presenting with septic shock, especially if high levels persist. Serial plasma lactate measurements are considered to be better indicators of organ failure and mortality than single lactate determination.(39)

Evaluation of lactate levels is mandatory to identify tissue hypoperfusion in children who are not yet hypotensive, but are at a high risk for septic shock.

Estimation of lactate levels in patients is not always straightforward.

For eg., elevated lactate levels may be due to decreased clearance by liver or lactic acidosis rather than global hypoperfusion. In the study by Ramzi et al, raised lactate (>3 mmol/l) and low bicarbonate (<17 mmol/l) at the onset of bacteraemia were found to be useful biomarkers in predicting mortality and septic shock in patients with neutropenia.(40) In a multivariate analysis, two variables-pulmonary infection and plasma lactate >3mmol/l were strongly associated with septic shock.

Procalcitonin

Calcitonin and its precursor procalcitonin (PCT) were used initially as serum markers for detection and follow-up of treatment for neuroendocrine tumours. Later, PCT levels were found to be elevated in patients with very severe systemic inflammation (e.g. systemic bacterial infection, trauma, and sepsis). Serum levels of procalcitonin are not detectable in healthy

individuals. (41)The production and biological function of procalcitonin involves complex and time-dependent mechanisms. Significant production of procalcitonin is observed in adherent monocytes, but not found in circulating leukocytes.Monocytes produce procalcitonin only for a limited time. Parenchymal cells produce procalcitonin after interaction with adherent monocytes. Systemic or local inflammations affecting parenchyma and monocyte adhesion are preconditions for procalcitonin production. This explains why PCT is induced by both local or systemic inflammation and tissue trauma. (42) Procalcitonin elevates rapidly (within 2-4 hours) in bacterial infections and severe forms of systemic inflammation. It has been shown in many settings that serum procalcitonin concentrations increase more rapidly than serum CRP concentrations in sepsis patients. In a recent review by Sakr et al,PCT was shown to differentiate fever due to systemic infection from fever of noninfectious causes.(43) PCT had only a minimal role in differentiating gram- positive from gram negative infections.

In a large meta-analysis, results were similar to the findings of Sakr et al. Though high procalcitonin occurred commonly in infection, it was also raised in many non-infectious conditions.(44)

Observations also showed febrile septic patients with documented bacteraemia having PCT values within normal range. Therefore, PCT is not a

specific indicator of either sepsis or infection and publications regarding its prognostic utility are contradictory. (45)

Interleukins

Interleukins (IL-6 &IL-8) are proinflammatory cytokines, mainly secreted by monocytes. They are an important part of the cytokine cascade, alongwith inhibitory cytokines. The kinetics of interleukins are very fast (releasing in less than 1-2 hours) but their concentrations may decline in a short period.IL-6 is a multifunctional cytokine which regulates T- and B-cell function and acute phase reaction such as CRP secretion. IL-8 is an inflammatory cytokine that chiefly functions as neutrophil activating factor and chemo-attractant. Engel et al have shown that both IL-6 and IL-8 have positive predictive value in neutropenic patients with bacteraemia.(46) Especially IL-8 has predictive capacity in this aspect. Anti-inflammatory cytokines, mainly interleukin 10(IL-10) and 4(IL-4), are produced to downregulate systemic inflammatory response (SIRS) in response to sepsis. The role of anti-inflammatory cytokines in various studies is rather obscure. Loisa et al studied anti inflammatory response in development of MODS in ICU setting, but overproduction of IL-10 was not seen.(47) In another study ,simultaneous identification of 17 different cytokines have shown that both anti- and pro- inflammatory cytokines were significantly elevated in patients

with septic shock rather than in patients with severe sepsis.Therefore, higher cytokine concentrations were found to be associated with severity and evolution of organ dysfunction, but anti-inflammatory cytokines have no specific role in this setting.

INTERNATIONAL CONSENSUS FOR PEDIATRIC SEPSIS-DEFINITIONS

Infection	Proven or suspected infection or a clinical syndrome with high probability of infection
Systemic inflammatory response syndrome (SIRS)	2 of 4 criteria, one must be abnormal leukocyte count or abnormal temperature : **1** Core temperature >38.5 C or <36 C (bladder, oral, rectal, or central catheter) **2** Tachycardia: Mean heart rate >2 SD above normal for age in absence of,chronic drugs, external stimuli or painful stimuli *OR*

	Unexplained persistent elevation lasting 0.5-4 hr *OR* In <1 year old, persistent bradycardia over 0.5 hour (mean heart rate <10th centile for age without vagal stimuli, β-blocker drugs, or congenital heart disease) **3** Respiratory rate >2 SD above mean for age or acute need for mechanical ventilation not related to general anesthesia or neuromuscular disease **4** Leukocyte count depressed or elevated for age (not secondary to chemotherapy) or >10% immature neutrophils
Sepsis	SIRS and a suspected or proven infection
Severe sepsis	Sepsis and 1 of the following: **1** Cardiovascular organ dysfunction,

	defined as:
	• Despite >40 mL/kg of intravenous isotonic fluid in 1 hour:
	• Hypotension <5th percentile for age or systolic blood pressure <2 SD below normal for age
	OR
	• Need for vasoactive agent to maintain blood pressure
	OR
	• 2 of the following:
	  • Unexplained metabolic acidosis with base deficit > 5 mEq/L
	  • arterial lactate: >2 times upper limit of normal
	  • Oliguria: urine output <0.5 mL/kg/hr

	• Prolonged capillary refill time: >5 sec • Core to peripheral temperature gap >3C **2** Acute respiratory distress syndrome (ARDS) as defined by the presence of a Pao_2/Fio_2 ratio ≤300 mm Hg, bilateral infiltrates on chest radiograph with no evidence of left heart failure *OR* Sepsis plus 2 or more organ dysfunctions (renal, respiratory, hematologic, neurologic, or hepatic)
Septic shock	Sepsis and cardiovascular organ dysfunction as defined above
Multiple organ dysfunction syndrome (MODS)	Presence of altered organ function such that homeostasis cannot be maintained without medical intervention

ETIOLOGICAL AGENTS

Fever of acute onset, with duration of <1 wk and without any localizing signs is a common diagnostic problem in children <36 mo of age. The etiology and evaluation of fever without localizing signs depends on the age of the child.

Traditionally, 3 age groups are considered:

neonates or infants to 1 mo of age,

infants >1 mo to 3 mo of age, and

children >3 mo to 3 yr of age.

In 1993, practice guidelines were published to help the clinician in evaluating an otherwise healthy 0 to 36 mo old presenting with fever without source. With the invention and widespread use of the conjugate *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* vaccines, the incidence of infections with these 2 pathogens have decreased markedly. As a consequence, changes to the 1993 guidelines have been advocated

IMMUNOCOMPETANT PATIENTS

Neonates (<28 days)	Sepsis and meningitis caused by group B streptococcus, *Listeria monocytogenes* ,*Escherichia coli*,; enteroviruses ,neonatal herpes simplex virus infection,
Infants 1-3 mo	Serious bacterial disease in 10-15%, including bacteremia in 5%; urinary tract infection
Infants and children 3-36 mo	Occult bacteremia in <0.5% of children immunized with both *Haemophilus influenzae* type b and pneumococcal conjugate vaccines; urinary tract infections
Hyperpyrexia (>40?C)	Meningitis, bacteremia, pneumonia, hemorrhagic shock-encephalopathy syndrome, heatstroke
Fever with petechiae	Bacteremia and meningitis caused by *H. influenzae* type b, *Neisseria meningitidis* and *Streptococcus pneumonia*

IMMUNOCOMPROMISED PATIENTS

Sickle cell disease	Sepsis, pneumonia, and meningitis due to *S. pneumonia* and osteomyelitis by *Salmonella* and *Staphylococcus aureus*
Asplenia	Bacteremia and meningitis caused by *H. influenzae* type b, *N. meningitidis* and *S. pneumonia*
Complement or properdin deficiency	Sepsis caused by *N. meningitides*
Agammaglobulinemia	Bacteremia, sinopulmonary infections
AIDS	*H. influenzae* type b, *S. pneumonia* and *Salmonella* infections
Congenital heart disease	brain abscess with right-to-left shunting Infective endocarditis
Central venous line	*Staphylococcus aureus*, , *Candida* coagulase-negative staphylococci
Malignancy	Bacteremia with gram-negative enteric bacteria, coagulase-negative staphylococci and *S. aureus*,; fungemia with *Candida ,Aspergillus*

ISOLATION

Isolation of the suspected bacteria is mainly based on culture.The best approach is to culture the entire volume of blood in a single aerobic bottle because anaerobic bacteremia is rare in children

ANTIMICROBIAL SUSCEPTIBILITY TESTS

Antimicrobial susceptibility tests are performed generally on all organisms with clinical significance except for few that have predictable antibacterial susceptibility patterns (eg.,group A streptococci universally remain susceptible to penicillin). The most common technique used is **agar disc diffusion method (Kirby –Bauer method)**, in which a standardized inoculum of organism is inoculated onto the agar plate. Then, antibiotic-impregnated filter paper discs are placed over the agar surface. After about 18-24 hr of incubation, the zone of inhibition against bacterial growth around each disc is measured and compared to nationally determined standards for resistance or susceptibility.

Another widely used technique for susceptibility is **dilution testing.** A standard concentration of the microorganism is seeded into serially diluted concentrations of the antibiotic, and **minimum inhibitory concentration (MIC)** in ug/mL, which is the lowest concentration of antibiotic needed to

inhibit growth of microorganism is determined. Dilution testing also allows the determination of **minimum bactericidal concentration (MBC),** which is the lowest concentration of antibiotic needed to kill the microbe. MBC is sometimes determined to eliminate the possibility of bacterial **tolerance** (MBC >4 times MIC)

ANTIBIOTIC USE IN CHILDREN AND ANTIBIOTIC RESISTANCE

Antibacterial therapy in infants and children presents several challenges. A daunting problem is paucity of data in children regarding pharmacokinetics and optimal dosages; unfortunately pediatric recommendations are therefore extrapolated from done in adults. A second challenge is the need for clinician to consider important differences between various age groups regarding the pathogenic species which are responsible for bacterial infections in children. Age-appropriate dosing of antibiotic and toxicity must be considered, taking into account the physiology and developmental status of infants and children. Finally, the style of antibiotics usage has several important differences compared to usage in adults.

Specific antibiotic therapy is driven optimally by **microbiologic diagnosis,** predicated based on isolation of pathogenic organism obtained from a sterile body site, and aided by antimicrobial susceptibility testing. Given the

inherent problems that arise in collecting specimens from children, and given higher risk of serious bacterial infection in young infants, most pediatric infectious disease management is based on a **clinical diagnosis** with **empirical** use of antibiotics before or even without final identification of the particular micro-organism.

Early administration of broad-spectrum antibiotics is associated with decreased mortality. The antibiotic choice depends on clinical situation and predisposing risk factors. Antibiotic resistance patterns in hospital and community must be considered in selection of appropriate antimicrobial treatment.

In infants and children, community-acquired infections by *Neisseria meningitidis* can be empirically treated with a 3rd-generation cephalosporin (cefotaxime or ceftriaxone) or high-dose penicillin.

H.influenzae infections can be empirically treated with a 3rd-generation cephalosporin (cefotaxime or ceftriaxone).

Prevalence of resistant *Streptococcus pneumoniae* very often requires addition of vancomycin, depending on specific clinical situation.

Suspicion of community- acquired or hospital-acquired, methicillin-resistant *Staphylococcus aureus* mandates coverage with vancomycin, depending on local resistance patterns.

In case an intra-abdominal process is doubted, anaerobic coverage with an antibiotic such as metronidazole, clindamycin, or piperacillin-tazobactam should be done.

Nosocomial sepsis can generally be treated with at least a penicillin with an extended gram-negative spectrum (e.g., piperacillin-tazobactam) or a 3rd- or 4th-generation cephalosporin. An aminoglycoside must be added as and when clinical situation warrants.

Vancomycin must be added to the treatment regimen in the following cases:

if the child has an indwelling medical device

2.if gram-positive cocci are isolated from culture

if methicillin-resistant *Staph aureus* infection is suspected

as empirical coverage for *S. pneumoniae* in a meningitis patients.

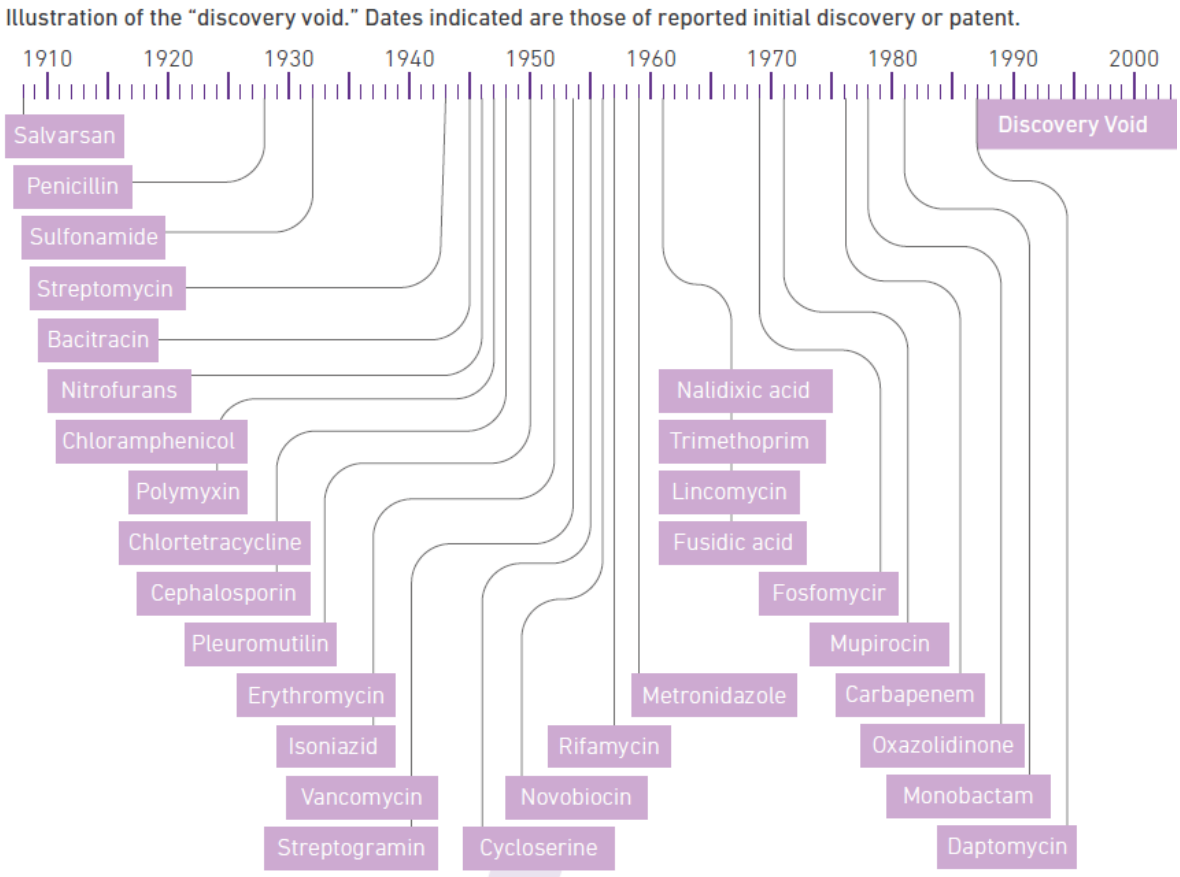
The above are generalized recommendations that must be tailored to individual clinical scenario and to local resistance patterns of the hospital or community.

For more than sixty years, antibiotics have been regarded as panacea to treat infections, whether their use is appropriate or not, and whether the infection was acquired in the community or in the hospital setting. In his Nobel Prize speech in 1945, Alexander Fleming, who discovered penicillin, had warned that bacteria would become resistant to the remarkable drugs called antibiotics. The development of each new antibacterial agent has been followed by detection of resistance. The development of resistance is considered a normal evolutionary process for microbes, but it is accelerated by selective pressure exerted by the widespread use of antibacterial agents. Resistant strains propagate and spread where there is non-compliance with control measures and infection prevention.

Use of antibacterial agents has become widespread over decades (although equal access to antibacterial agents is not being available worldwide), and also these are extensively being misused in both humans and animals in ways that favour the selection and spread of resistance.As a result, antibacterial drugs are less effective or even ineffective, resulting in accelerating global

health security emergency which is outpacing available treatment options rapidly.

Until 1970s, many new antibacterial drugs were discovered to which most of the common pathogens were fully susceptible initially, but the latest completely new classes of antibacterial agents were discovered during 1980s



Antibiotic resistance has developed as an alarming problem in child-care, because incidence of infection by organisms resistant commonly used

antimicrobial drugs has dramatically increased. The estimated annual rate of antibiotic usage among children in hospitals is 2 to4 times higher than in age-matched children cared at home and the average duration of treatment is 4 times longer amongst children in child care. This high frequency of antibiotic usage combined with propensity for person-to-person transmission of microbes in a crowded environment resulted in an increased prevalence of antibiotic-resistance in bacteria of the respiratory and intestinal tracts, including *S. pneumoniae, Moraxella catarrhalis, H. influenzae,* , *Shigella* species and *E. coli* O157:H7.

WHY IS ANTIMICROBIAL RESISTANCE A GLOBAL PROBLEM?

Antimicrobial resistance (AMR) kills

Challenges care and control of infectious diseases

Greatly increases care costs

Threatens a return to the pre-antibiotic era

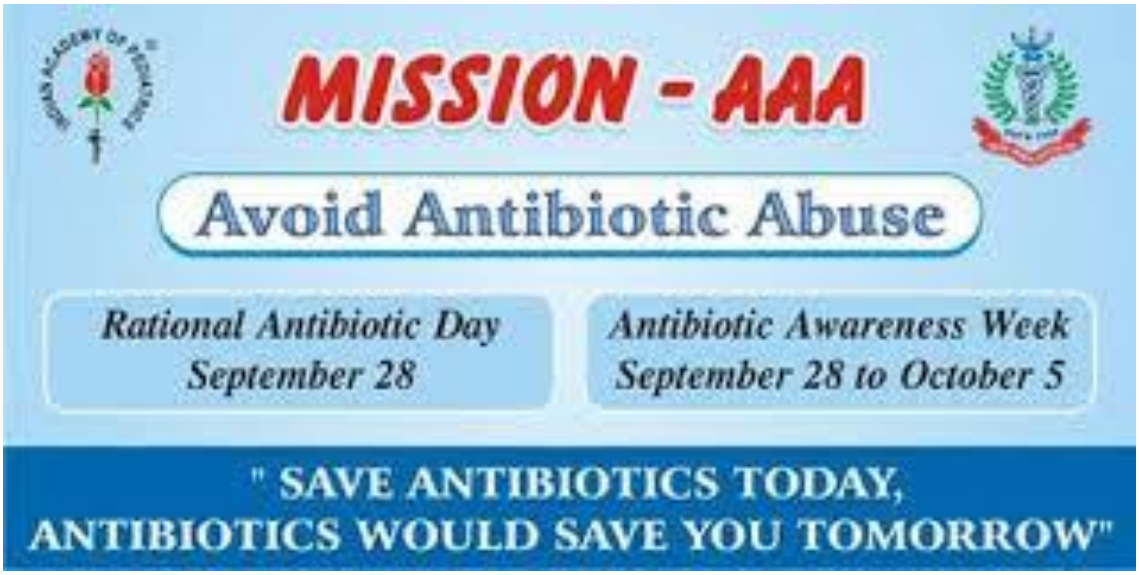
Jeopardizes healthcare gains for individuals and society

Compromises health security, damages trade and economy

Lack of coherent approaches to prevention and containment

AVOID ANTIBIOTIC ABUSE (AAA)

Fostering awareness about antimicrobial resistance and rational antibiotic practice is a part of the IAP ICMR Call to Action declared this year. As a commitment to reduce antibiotic misuse, September 28 will be observed as the Rational Antibiotic Day and the week thereafter, has been declared as Antibiotic Awareness Week. September 28 has been selected in commemoration with Sir Alexander Flemming's discovery of penicillin.



PREVENTION OF SEPSIS

There is increased focus on the prevention of nosocomial infections.This is well emphasized by the fact that five of the sixteen elements of Joint Comission's National Patient Safety Goals (2009) relate directly to prevention of health

Care–associated infection (HAI),being

1.hand hygiene

2.major permanent loss of function following HAI or unanticipated death

3.surgical site infections

4.central line associated bacteremia

5.infections caused by multi-drug resistant organisms

STEPS FOR PREVENTIONS OS SEPSIS

The most important method in any infection control is to practise good hand hygiene.Hands must be cleaned during every patient meeting. **Waterless hand hygiene** increase hand hygiene compliance and also save time; these hand hygiene agents are preferred for routine hand hygiene .Universal precautions includes use of the following-gloves, goggles, gowns, masks, and face shields—for preventing transmission of micro organisms which can be transmitted via blood and body fluids..

Isolation of patients as and when needed decreases the risk of transmission of microbes to other patients and health care personnel.

Aseptic precautions must be followed during all invasive procedures and intravenous and central line catheter placements. The barrier during catheter

placement decreases risk of microbial transmission almost by half. It is necessary to remove unnecessary catheters as soon as possible

Immunization with conjugate *H. influenza* type b and *S. pneumonia* is recommended for all children. High-risk patients in addition must receive conjugated pneumococcal vaccine, 23-valent pneumococcal vaccine,and also quadrivalent meningococcal vaccine(groups A, C, Y, W-135) at two years of age.

In patients with functional asplenia (e.g., sickle cell anemia) and anatomical asplenia penicillin prophylaxis is recommended.

In house hold contacts of patients with meningococcal disease or invasive H.influenza disease prophylaxis is recommended.

REVIEW OF LITERATURE:

STUDY1:WHO REPORT ON ANTIMICROBIAL RESISTANCE 2014:

Antimicrobial resistance (AMR) in a wide range of infections is a growing public health threat both to countries and multiple sectors.

Determining the scope of this problem is of utmost importance for monitoring and formulating an effective response to AMR. The WHO report which is produced in collaboration with the member States and various other partners, provides an accurate idea of the magnitude of AMR and also the current state of global surveillance .

Bacteria commonly causing infections in hospitals and in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data	No. of WHO regions with national reports of 50% resistance or more
Escherichia coli/	Urinary tract infections, blood stream infections		
- vs 3rd gen. cephalosporins		86	5/6
- vs fluoroquinolones		92	5/6
Klebsiella pneumoniae/	Pneumonia, blood stream infections, urinary tract infections		
- vs 3rd gen. cephalosporins		87	6/6
- vs 3rd carbapenems		71	2/6
Staphylococcus aureus/	Wound infections, blood stream infections		
- vs methicillin "MRSA"		85	5/6

Bacteria mainly causing infections in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data	No of WHO regions with national reports of 25% resistance or more
Streptococcus pneumoniae/ - non-susceptible or resistant to penicillin	Pneumonia, meningitis, otitis	67	6/6
Nontyphoidal Salmonella/ - vs fluoroquinolones	Foodborne diarrhoea, blood stream infections	68	3/6
Shigella species/ - vs fluoroquinolones	Diarrhoea ("bacillary dysenteria")	35	2/6
Neisseria gonorrhoea/ - vs 3rd gen. cephalosporins	Gonorrhoea	42	3/6

The high proportion of resistance to the 3rd generation cephalosporins for *K.pneumoniae and E.Coli* means that the treatment of severe infections caused by these in many clinical settings must rely on carbapenem group of antibiotics,considered the last resort to treat severe hospital and community acquired infections.

Of concern is the fact that *Klebsiella pneumoniae* resistant to carbapenems also has been identified in most countries that provided data with resistance up to 54% reported.

High rates of MRSA mean that treatment for suspected /verified severe *Staph aureus* infections, like common skin and wound infections should rely on secondline agents. Second-line agentsfor *S. aureus* are very expensive; And they have severe side-effects needing monitoring during treatment,which increases costs even further.

Reduced susceptibility to penicillin has been detected in *Streptococcus pneumoniae* in all WHO regions, exceeding 50% in some reports.

The resistance to quinolones among two of the major causes for bacterial diarrhea namely*Shigella species* and nontyphoidal *Salmonella* (NTS) were found to be comparatively lower than in *E. coli*.

Among a wide range of WHO initiatives, in 2001 *Global strategy for containment of antimicrobial resistance* was published, and antimicrobial resistance(AMR)was the main focus of World Health Day 2011 when a 6-point antimicrobial resistance(AMR) policy package was issued

1.Commitment to comprehensive, financed national plan with civil society engagement and accountability

2.Strengthening surveillance and laboratory capacity

3.Ensuring an uninterrupted access to essential medicines of assured

quality

4.Regulating and promoting rational use of antibiotics including animal husbandry and ensuring proper patient care

5.Enhancing infection prevention and control

6.Fostering innovations and also research and development for new tools

RESISTANCE DATA ON SPECIFIC PATHOGENS

ESCHERICHIA COLI – resistance to 3rd-generation cephalosporins and to fluoroquinolones *E. coli* is part of normal flora of intestine in humans and animals. Nevertheless it is the most frequent etiological agent of community and hospital acquired urinary tract infections :the most frequent cause of bloodstream infections at all ages; associated with many intra-abdominal infections such as peritonitis, also skin and soft tissue infections due to multiple microorganisms; cause of neonatal meningitis :one of leading causative microbe of food borne infections worldwide.

E. coli infections usually originate from the person who is affected (auto-infection), but then strains with a specific resistance or disease-causing properties are also transferred from animals, between individuals or through food chain.

Resistance in *E. coli* develops readily either through **mutations**, often the case for fluoroquinolone, or acquisition of mobile genetic elements, which is the case for broad spectrum penicillins (e.g. amoxicillin or ampicillin) and also resistance to third-generation cephalosporins.

Resistance to 3rd -generation cephalosporins is conferred mainly by **enzymes** called extended spectrum beta-lactamases (ESBLs); these destroy many beta-lactam antibiotics.

ESBLs can be transmitted between bacteria and between bacterial species. As the ESBL containing *E. coli* strains are also resistant to various other antibacterial drugs, carbapenems remain the only available option for severe infections. A recent threat is emerging carbapenem resistance in E. *coli* caused by metallo-betalactamases,that confers resistance to almost all available beta-lactam antibiotics.

The WHO report focus is on available data on proportions of *E. coli* that are resistant to third-generation cephalosporins, widely used for intravenous treatment of severe sepsis in hospitals, and also to fluoroquinolones,that are among the widely used oral antibiotics in the community setting.

The resistance reported to fluoroquinolones seemed generally higher than for third-generation cephalosporins. Similar to resistance to the 3rd generation

cephalosporins, there also were reports of resistance to fluoroquinolone in *E. coli* exceeding 50% in five WHO regions.

KLEBSIELLA PNEUMONIAE – resistance to carbapenems and third-generation cephalosporins Similar *to E.coli*, bacteria of *Klebsiella* genus are frequent gut colonizers in humans and vertebrates. *K.pneumoniae* infections are common particularly in hospitals invulnerable individuals like pre-term infants and immmunocompromised patients, diabetes or alcohol-use disorders, and receiving advanced medical care.

The most common infections are respiratory tract and urinary tract infections and, in neonates,they cause bloodstream infections. *Klebsiella pneumoniae* is one of the common causes of Gram-negative septicemia. The mortality rates for *Klebsiella pneumonia*e hospital-acquired pneumonia depends on severity of underlying condition, and can go beyond 50% in vulnerable patients, though treated with appropriate antibiotics.

Similar to other bacteria in health-care settings. *Klebsiella pneumoniae* spreads readily between patients, causing nosocomial outbreaks. Frequently, this occurs in intensive care units and newborn care facilities.. *K. pneumoniae* spread among different hospitals and across country borders via transfer of colonized or infected patients has also been documented .

EVOLUTION OF ANTIBACTERIAL RESISTANCE IN *KLEBSIELLA PNEUMONIAE*

Like E. coli, K. pneumoniae acquires resistance to various antibacterial drugs mainly via horizontal transfer of genetic elements such as plasmids or transposons. Unlike *E. coli*, *K. pneumoniae* carries resistance gene (betalactamase located in chromosome) that naturally renders penicillins with extended spectrum, like ampicillin and amoxicillin ineffective. Resistance to various other widely used oral antibacterial drugs like fluoroquinolones (e.g. ciprofloxacin) and cotrimoxazole has arisen and spread globally. This means that there are very few remaining options for oral antibiotics for Klebsiella infections in several parts of the world.

In 1982, the world's first ESBL *K. pneumoniae* was identified during hospital outbreak *of K. pneumoniae* infections in Germany. Since then about 200 different ESBL variants have been identified, which have spread rapidly worldwide. Moreover, various ESBL variants identified initially in *K. pneumoniae* have transferred subsequently to *E. coli*. ESBL-producing strains are resistant to all beta-lactam antibacterial drugs such as cephalosporins and so for these strains, carbapenems are the main treatment option remaining.

Worldwide, *Klebsiella pneumoniae* is the main cause of infections caused by carbapenem-resistant bacteria.All of the important genes which confer carbapenem resistance (mediated via carbapenemases) are present in *K. pneumoniae*, therefore rendering almost all treatment options available ineffective. For patients infected with these carbapenam resistant bacteria there are no treatments effective clinically.

Majority of sources have reported more than 30 percent resistance among *K._pneumoniae* against 3rd-generation cephalosporins, and in some countries more than 60%.

Very alarming rates of carbapenem resistance almost exceeding 50% have been reported in *Klebsiella pneumonia*e in some patients, for which few alternative treatment options are available.

***STAPHYLOCOCCUS AUREUS* –**methicillin resistance

Staph aureus is a gram-positive bacterium which can be a part of normal flora of the skin and the nose, but is one of the most important pathogens in humans.

Staph aureus causes a variety of infections, notably soft tissue, skin, bone and bloodstream infections. *Staph aureus* is also the most common cause of wound infections postoperatively. Some *S.aureus* strains produce toxins

which can cause a wide variety of specific symptoms that includes food poisoning and toxic shock syndrome.

EVOLUTION OF ANTIBIOTIC RESISTANCE IN *STAPHYLOCOCCUS AUREUS*

When penicillin was introduced first, it was an effective treatment for *Staph aureus* infections, but already resistance had developed during 1940s. The resistance was mediated mainly by the production of betalactamase enzyme which inactivates drugs like penicillin, amoxicillin and ampicillin. Consequently,beta-lactamase-stable drugs (e.g. cloxacillin and methicillin) as well as beta-lactamase inhibitor(e.g. sulbactam and clavulanic acid)which could be combined with antibacterial drugs were developed.

S.aureus strains resistant penicillinase stable antibacterial drugs have acquired a new gene (mecA) which codes for novel penicillin-binding protein(PBP); such strains are called methicillin-resistant *Staphylococcus_aureus* (MRSA).

The very first strains of MRSA emerged during 1960s. MRSA was initially a problem in hospital-acquired infections only. However, over the past decade, community-acquired MRSA(ca-MRSA) has significantly increased in various countries. Fortunately though, many of the community-acquired MRSA have so far retained susceptibility to various non-beta-lactam

antibiotics, whereas most of the health-care associated MRSA are difficult to treat multidrug resistant strains. For the latter group, treatment of last resort is glycopeptides antibiotics like vancomycin (since 1950s) and teicoplanin, that can only be given by intravenous route and also requires careful monitoring to avoid adverse drug reactions.

New treatment options for MRSA (but are associated with problematic side effects) have been developed recently: linezolid(since 1970s) and daptomycin (since1980s) are the recently licensed antibiotic drugs.

Data on MRSA among *S. aureus* were got from 85 (44%) of the WHO Member States.

Most of the reported MRSA proportions exceed 20% in all regions of WHO, and even exceeds 80% in some of the reports.

STREPTOCOCCUS PNEUMONIAE -RESISTANCE (OR NON-SUSCEPTIBILITY) TO PENICILLIN

Worldwide, *S. pneumoniae* (these bacteria are also called pneumococi) is the protean cause of community-acquired pneumonia, which is the main killer disease of children less than 5 years of age. Other diseases due to *S. pneumoniae* include, self-limiting infections like acute otitis media, but it also extends to cases of invasive pneumococcal disease with very high mortality rates such as meningitis. Amongst bacterial causes of meningitis,

pneumococci is associated with highest case–fatality rate and it is the most likely to leave survivors behind with permanent residual symptoms and sequele.

The clinical burden of *S. pneumoniae* infection is concentrated in the youngest and eldest sections of population. According to an estimate, pneumococci caused around 826 000 deaths (582 000—926 000) in children of age group 1—59 months.In HIV-negative children *S. pneumoniae* infection accounts to 11% of deaths in this age group .

Pneumococci are found commonly in asymptomatic nasopharyngeal carriage, the prevalence varies by age and region. Asymptomatic carriage state is responsible for most of the transmission inside populations, like day-care centres.

EVOLUTION OF ANTIBACTERIAL RESISTANCE IN *STREPTOCOCCUS PNEUMONIAE*

Beta-lactam drug resistance in clinical isolates of pneumococci occurs via the acquisition of mutations in genes coding for penicillin binding proteins (PBPs), which are the essential components of bacterial cell wall. The successive acquisition of several mutations in different PBPs results in an increasing minimum inhibitory concentration (MICs) for penicillin and the other beta-lactam antibiotics.

NONTYPHOIDAL *SALMONELLA* –RESISTANCE TO QUINOLONES

Bacteria of genus *Salmonella* are one of the major causes of foodborne infections throughout the world. Being a zoonotic pathogen, *Salmonella is* found in the intestine of several food-producing animals like poultry and pigs. Usually, infection is acquired by consumption of contaminated food or water or of animal origin: chiefly undercooked meat, eggs ,poultry and milk. Animal or human faeces also contaminate the surface of vegetables and fruits, leading to foodborne outbreaks.

Most of the *Salmonella* strains cause gastroenteritis, whereas some strains,in particular *Salmonella enterica* serotypes namely Typhi and Paratyphi, are more invasive and therefore cause the typical enteric fever. Enteric fever is more serious infection that poses problem regarding treatment because of antimicrobial resistance in several parts of the world.

EVOLUTION OF ANTIMICROBIAL RESISTANCE IN NONTYPHOIDAL *SALMONELLA*

Antimicroial resistance varies between various serotypes of nontyphoidal *salmonella,* and this is significant in some of them. In the late1990s and early 2000s, various clones of multidrug resistant *Salmonella have* emerged, and then they have expanded worldwide. For example, in *Salmonella enteric*

typhimurium,the genomic element which carries resistance to five different antimicrobials (ampicillin, chloramphenicol,streptomycin, tetracycline and sulfonamides) spreads horizontally among the other serotypes and acquires additional resistant determinants.

STUDY 2;

Pediatric antimicrobial susceptibility trend across the United States Of (2005-2011)-Tamma et al

Carbapenems were the most effective antibiotics against gram negative organisms but did not have over 90% coverage against Pseudomonas.Incidence of MRSA was 50%.The indicence of MRSA was lower in western districts.Resistance to clindamycin was seen in 21% of S.Aureus.. Enteroccus faecium showed 25% susceptibility to ampicillin and 45% to vancomycin.Linezolid resistance was seen in 8% of E. faecium. Southern hospitals reported higher E. faecium prevalence with susceptibility to vancomycin, ampicillin, and linezolid compared to other 3 regions (P< .01).(50)

STUDY 3:

Pediatric bloodstream infections , Cambodia, 2007 to 2011(Stoesser et al)

Of 7682 blood cultures with results , 606 (7.9%) BSI were found in 588 children.Increase of incidence of blood stream infections from 14/1000 to 50/1000 was attributed to increasing sampling.Most of the infections was acquired from community(89.1%). Common pathogens were S. Typhi (22.8%), Staph aureus (12.2%), S.pneumoniae (10.0%), Klebsiella (6.4%) and E.coli (6.3%). 21.5% of sepsis was due to unconventional gram negative organisms. Listeria monocytogenes and Group B streptococci were not identified.Antibacterial resistance was increased more so in the enterobacteriaceae family. Overall the mortality was high(19.0%), highest in newborn (36.9%) (51)

STUDY 4

Staph aureus infections in children in Iranian tertiary pediatric hospital- by Sabouni et al(2011-2013)

During the study period ,the percentage of MRSA infections of all S. aureus isolated was 79% (77/98). Additionally, 58/74 (78%) were identified to be Hospital- Acquired Methicillin Resistant S. aureus (HA-MRSA) and the

remaining 20/24 patients (83%), were identified as Community-Acquired Methicillin-Resistant S. aureus (CA- MRSA).(52)

STUDY 5

Bacteriological profile and antibiogram of isolates of blood culture from a children hospital in Kabul-Tariq et al(2010-2012)

Positive blood culture rate was 12.2%. Of the total 410 isolates, 212 (51.71%) gram-negative bacilli and 184 (44.88%) gram-positive cocci were isolated. Additionally, 14 (3.41%) Candida spp were isolated. Most species of gram-negative bacteria isolated were Enterobacteriaceae and included 66 K.pneumonia (16.1%), 42 Enterobacter (10.2%), 35 E. coli (8.5%) and 16 Serratia (3.9%) spp. 21 (5.12%) Pseudomonas species were isolated. Of the gram-positive cocci isolated, most were coagulase-negative Staphylococci (26.34%) andStaphylococcus aureus (11.95%) ,Streptococcus species (5.12%). Of the ESBL producing organisms 51.9% were multidrug-resistant and had resistance to Ampicillin, Gentamicin, , Fluoroquinolones, 3rd gen Cephalosporins and Co-trimoxazole. Most were sensitive to Imipenem (200/212, 94.3%), Amikacin (172/212, 81.1%) ,Fosfomycin (166/212, 78.3%).Of the gram-positive cocci, most isolates were resistant to Gentamicin, Penicillin, 3rd gen Cephalosporins, quinolones and Cotrimoxazole. Most isolates were found to be sensitive to Pristinamycin

(161/184, 87.5%) Vancomycin (183/184) and Fosfomycin (134/184, 72.8%). All S.aureus were resistant to penicillin and 51% of the isolates were MRSA.(53)

STUDY 6

A study on bacteriological profile ,antibiogram of organisms causing bacteremia in children less than 10 years in referral hospital in bangalore, India-Tiwari et al

Of the 128 suspected cases, 32 (25%) were culture positive. Male: female ratio was 1.28:1.0. Klebsiella (43.75%) was the most common bacteria and next was Staphylococcus aureus (18.75%). The prevalence of gram negative bacteria was 71.87%. Most gram negative bacteria maximum resistance to ampicillin and the gram positive bacteria to penicillin. Three gram negative bacteria produced extended-spectrum beta lactamases (ESBLs) and 1Pseudomonas aeruginosa produced metallo-beta lactamase (MBL).Incidence of MRSA among S.Aureus isolates was 33.33%.(54)

Our study is attempt to find out the bacterial agents for sepsis and their sensitivity/resistance patterns for our local prevalence of infections in our hospital to rationalize optimum antibiotic usage

OBJECTIVES:

1.To isolate and identify bacterial etiological agents responsible for sepsis in children aged 1-36 months

2.To determine the susceptibility patterns of isolates

METHODOLOGY

STUDY DESIGN: Prospective descriptive study

STUDY PLACE: Institute of child health, egmore, chennai

STUDY PERIOD: Mar 2014- Sept 2014

STUDY POPULATION: All children in age group 1-36 months with suspected bacteremia*

CASE DEFINITION

INCLUSION CRITERIA: All children in age group 1-36 months with sepsis (pediatric consensus on sepsis) and suspected bacteremia*(48)

Any child 1-36 months toxic appearing and temp >= 38 deg celsius

Any child 1-36 months presenting with septic shock/severe sepsis

1-3 months temp >=38 deg celsius with exclusion of low risk infants

3-36 months temp >=39 deg celsius

EXCLUSION CRITERIA:

Chidren appearing non toxic

Infants 3-36 months with low risk i.e.

Uncomplicated history

Normal physical examination

Normal lab parameters

WBC 5000-15000 cells/cumm

Urine WBC less than 10/hpf

Stool if diarrhoea (no RBC and WBC less than 10/hpf)

SAMPLE SIZE: 300

MANOEUVRE:

Children fulfilling the criteria for inclusion in study enrolled.

Informed consent obtained from parents.

About 2 ml of blood collected by sterile technique(skin disinfected with alcohol and povidone iodine)

SKIN ANTISEPSIS.

The likelihood of the isolate from blood culture being a true isolate rather than a contaminant depends on the degree os skin antisepsis. The recommended antiseptics are 70% isopropyl alcohol,and an iodine tincture or iodophor..

Blood collected in BHI broth for initial culture by automated blood culture directly via a syringe and inoculated into the bacT/ALERT culture media under strict asepsis.

PRINCIPLE OF THE TEST

BacT/Alert: an Automated Colorimetric Microbial Detection System

The BacT/ALERT Microbial Detection is based on the principle of colorimery in that there is detection of CO2 production by the micro organism which gets dissolved in the media as the organism utilizes the media.The CO2 produced is detected via a light permeable sensor located at bottom of the bottle indicated by a color changr from blue green to yellow

The light color causes an increase of reflectance units which is monitored by the system. The color reflectance is monitores every 10 minutes

BacT/ALERTÆ PF (coded yellow) :

BacT/ALERT PF culture bottles contain 16ml of complex

media and also 4ml of a charcoal with average density of 1.0215 g/mL. The media onsists of brain heart infusion solids (0.1% w/v), soybean-casein digest (2.0% w/v), sodium polyanethol sulfonate (SPS) (0.025% w/v), , menadione (0.0000625% w/v), L-cysteine (0.025% w/v), pyridoxine HCI (0.001% w/v)hemin (0.000625% w/v), and complex carbohydrate and amino acid substrates in water. Bottles contain CO2 atmosphere

in O2 and N2 under vacuum.

BACT/ALERT PF SYSTEM

After the culture bottles are loaded into instrument, they are incubated 5-7

days until declared positive.

3. All positive bottles are smeared and sub cultured.If they are false positive they are reloaded in the instrument until deemed positive.

4. Negative bottles are checked by smear and subculture before being discarded as negative.

Interpretation of Positive Cultures

Parameters that help in interpreting results are

1.The identity of the microorganism,

2.Presense of the same organism in more than one blood culture

3.Presence of same microbe in an another normally sterile body site

Microorganisms which mostly (>90% of isolates) represent true infection include *Escherichia coli* ,*Staphylococcus aureus,* and other Enterobacteriaceae, S.*pneumoniae, P. aeruginosa,* and *Candida albicans.*

Isolates which rarely «5% of isolates) represent true infection are *Bacillus* species, *Corynebacterium* species, and *Propionibacterium acnes.*

LIMITATIONS

Certain strains of Neisseria meningitidis, Neisseria gonorrhoeae, Haemophilus influenzae, and Peptostreptococcus are sensitive to the anticoagulant SPS which results in low production of CO2 culture bottles in case of insufficient blood inoculation.

BacT/ALERT positives may de due to high WBC count.In such cases,further subcultures and smears are negative

Some pnemococcal strains may get autolysed if they are not subculutures immediately

A Gram-stained smear from negative bottle may contain small number of non-viable microbes derived from staining reagents, immersion oil, culture medium components, or glass slides.

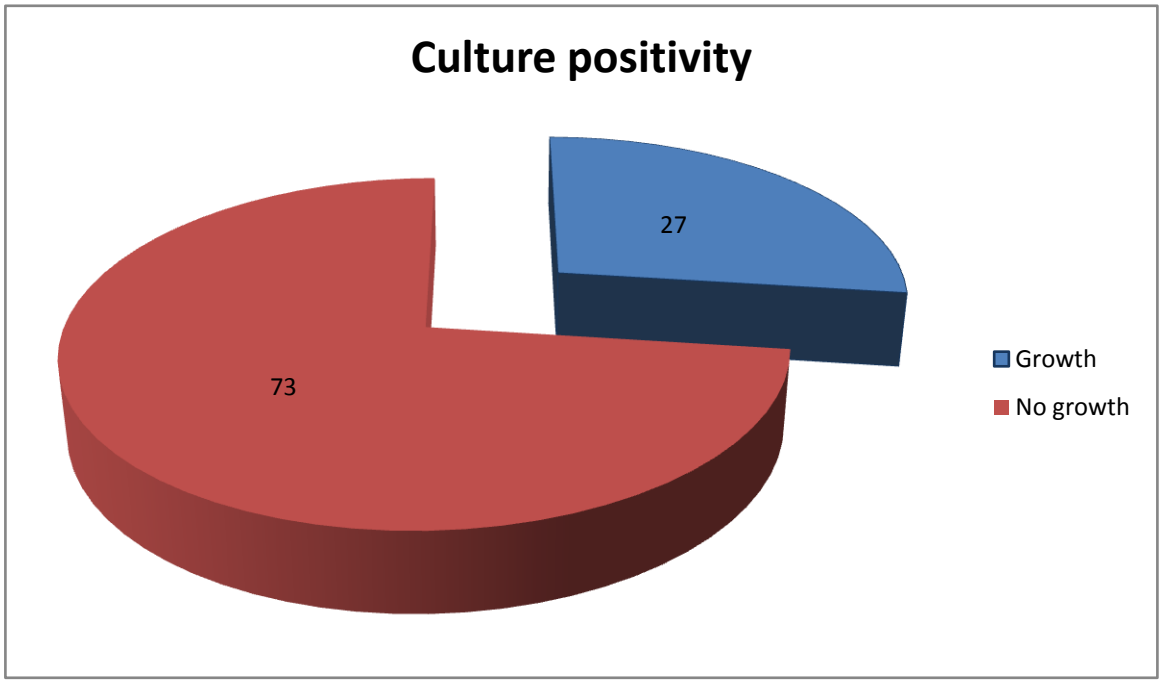
Further subcultures on specific media were done based on the organisms isolated .

The antibiotic susceptibility was done based on KIRBY-BAEUR disc diffusion method using standard MIC’s for the specific organism and the antibiotic used.

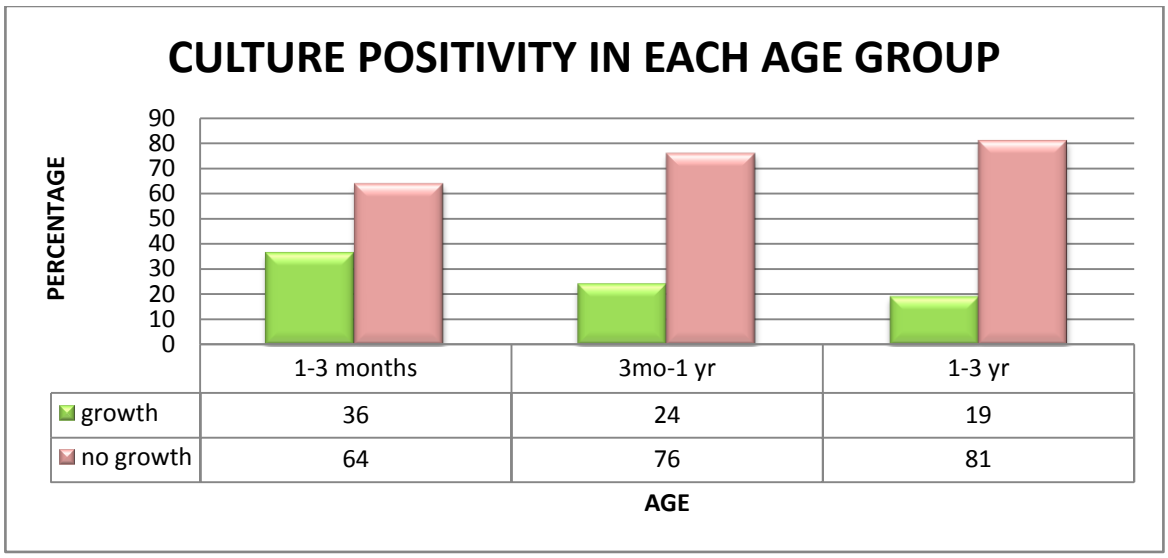
RESULTS

CULTURE POSITIVITY

Overall positive cultures were obtained in 80 cases among the total 300 cases selected for the study yielding a culture positivity rate of 27% overall.



CULTURE POSITIVITY –AGE WISE



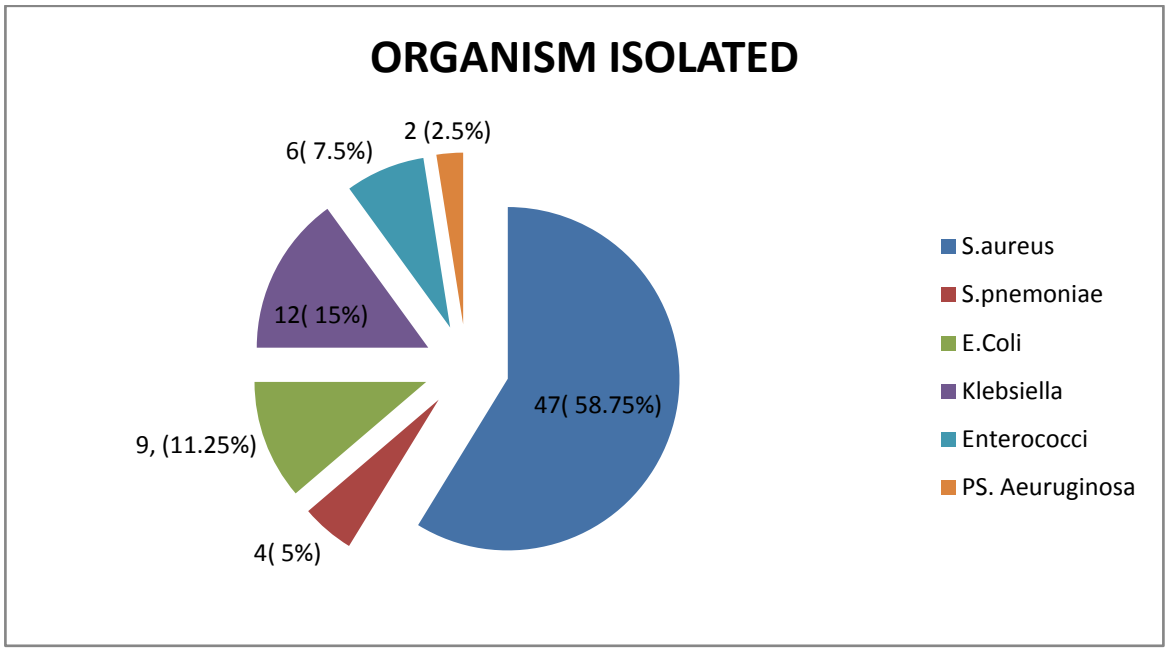
From the above chart it can be seen that the maximum culture positivity is in the age group 1-3 months where the culture positivity rate is 36% whereas the culture positive rate in age group 1-3 yrs is only 19 % indicating higher prevalence of bacteremia in younger age group.The isolation rate among age 3 months to 1 year is 24%.

ORGANISMS ISOLATED

The most common organism isolated was Staphlococcus aureus.it was isolated from 47 cases-accounting for 58.75 % of culture positive cases.

The next most common organism was Klebsiella pneumonia which was isolated from 12 pcases(15% of total culture positivity).

E.Coli was isolated in 9 children(11.25%),Enterococci in 6 cases(7.5%),Streptoccous pnuemoniae in 4 cases(5%) and Pseudomonas aeruginosa in 2%(2.5%)



AGE WISE DISTRIBUTION OF ORGANISMS ISOLATED

AGE-WISE ORGANISM PRESENT (IN NUMBERS)							
			ORGANISM				
Age-group	PHEUMO	STAPH	EC	KL	ENT	PS	TOTAL
1-3 M0	3	22	6	5	2	0	38
3 M0 - I Yr	1	14	2	4	3	0	24
1Yr-3Yrs	0	11	1	3	1	2	18
Total	4	47	9	12	6	2	80

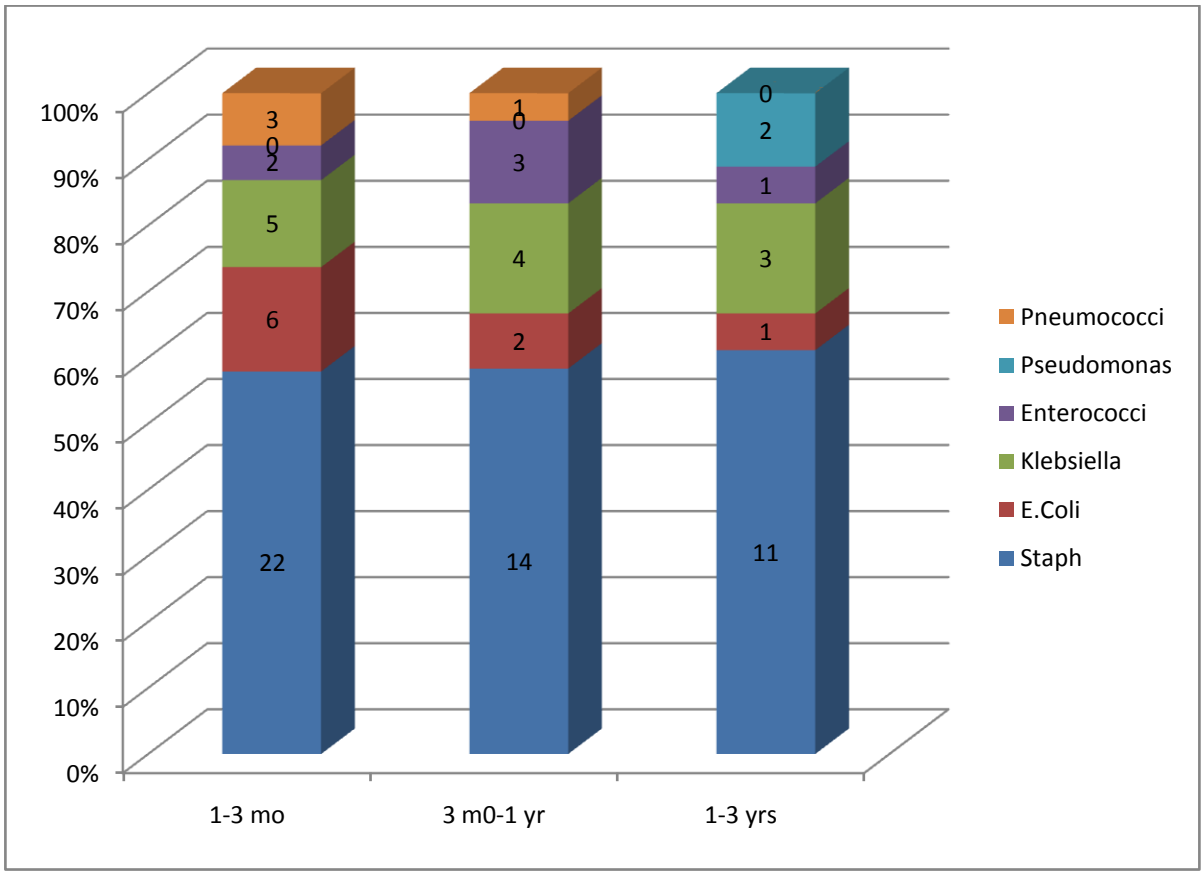
It can be seen that the most common organism in all age groups is Staphylococcus aureus,contributing to 58% among organisms grown in 1-3 months,58% in age 3 months to 1 yr and 6% in age 1-3 y.rs respectively

Of the pneumococci grown 75% were grown in age group 1-3 months.

Two pseudomonas grown were in the age group 1-3 years.Both the children were immunocompromised.

The second most common organism in the age groups 1-2 months,3 mo-1 yr and 1-3 yrs are E.Coli,Klebsiella and Klebsiella respectively

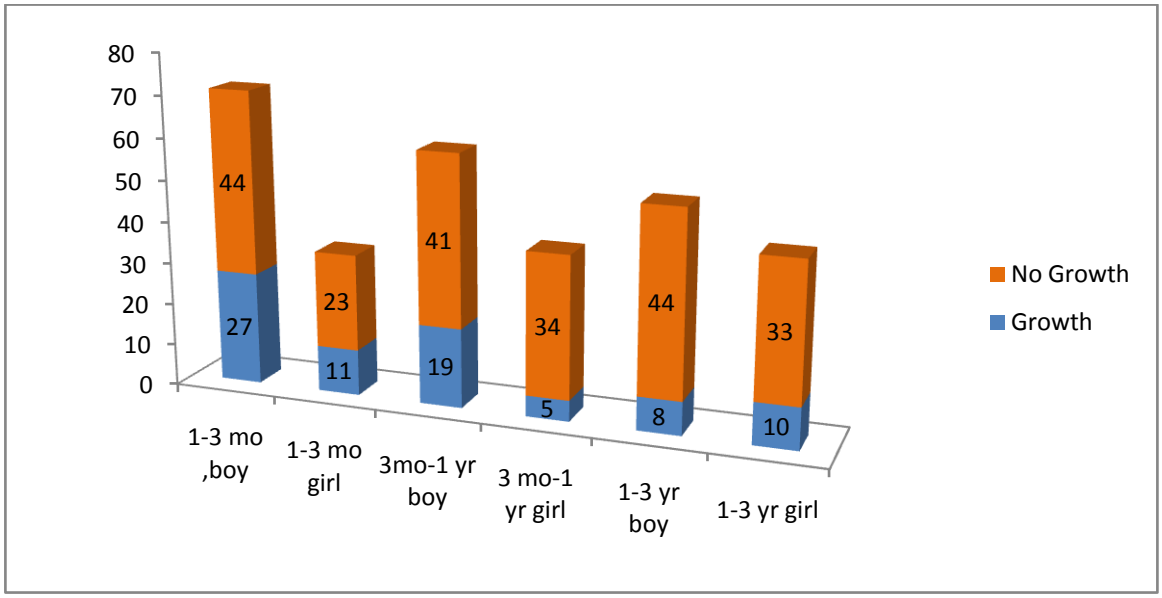
AGE WISE DISTRIBUTION OF ORGANISMS



SEX DISTRIBUTION OF CULTURE POSITIVITY

AGE AND SEX-WISE GROWTH AND NON-GROWTH						
	GROWTH		NON-GROWTH		TOTAL	
AGE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
1-3 M	27	11	44	23	71	34
3 M - I Yr	19	5	41	34	60	39
1Yr-3Yrs	8	10	44	33	52	43
TOTAL	54	26	129	90	183	116

Of the 300 children selected,183 were boys and 111 were females.The culture positivity rates in boys was 29%(54/183) and among girls was 22%(26/116).(P>0.05).No significant statistical difference was noted in the isolation rates between boys and girls.



EFFECT OF BREAST FEEDING ON CULTURE POSITIVITY

Among the culture isolated cases,in the age group 3 mo-1yr and 1-3 yrs,14.28% and 28.57% were exclusively breast fed upto six months.

In the age group 1-6 months,Yes/No was considered on the basis of whether the infant was being exclusively breast fed or not.

Where as among the non-growers the % of breast feeding was significantly higher-around 85% and 72% in the age group 3 mo -1 yr and 1-3 yrs respectively.(P>0.05)

AGE	BREAST FEEDING - AGE-WISE GROWTH AND NO GROWTH				TOTAL
	GROWTH		NON-GROWTH		
	BREAST FEEDING		BREAST FEEDING		
	Y	N	Y	N	
1M-3M	20(52%)	19	54	13	106
3M-1YR	3(14.28%)	21	69	6	99
1YR-3YRS	4(28.57%)	14	71	6	95
TOTAL	27(48%)	54	194	25	300

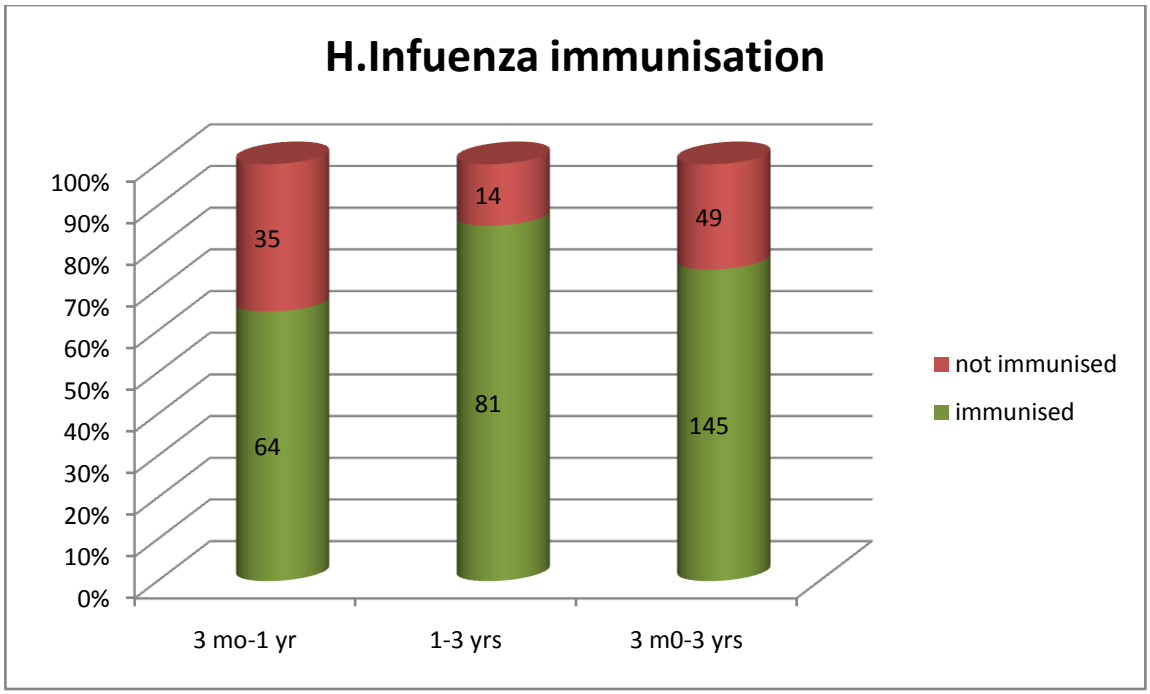
IMMUNISATION

We considered only immunization against bacterial agents known to cause sepsis.The two organisms being H.Influenza and Pneumococci.

None of the children chosen in our study had received Pneumococcal vaccine as it is not covered in the national immunization schedule and all our children had received their primary immunization in the government set up.

H.influenza B vaccine was integrated in the immunization schedule as the pentavalent vaccine since December 2012.In our study it was found that above the age group of 3 months(where the children are likely to have completed their immunization schedule against H.Influenza) 74.74% had received all three doses.Obviously,none of the infants below 3 months have completed their three doses of H.Infuenza vaccine

This introduction of H.Infuenza vaccine has a major impact on isolates as there are no isolates of H.Influenza among the culture positive cases.

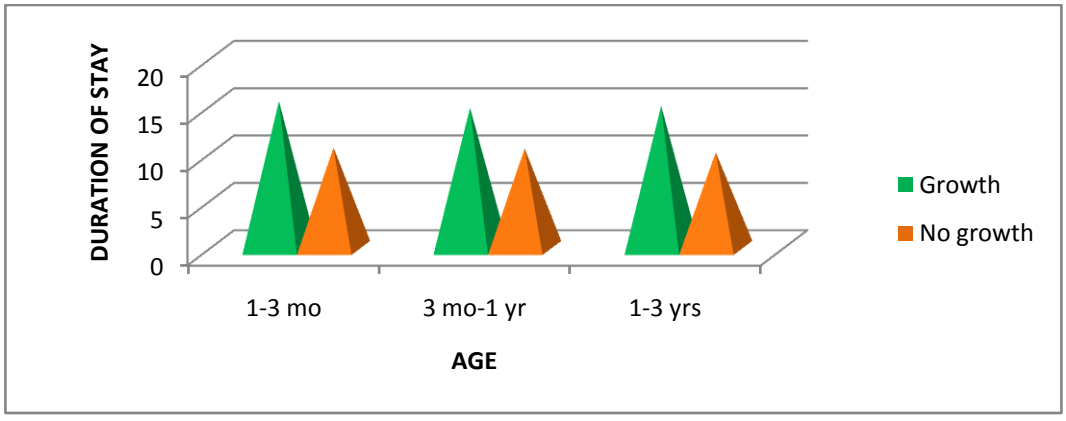


AGE	AGE-WISE IMMUISATION		
	IMMUNISATION		
	Y	N	TOTAL
1M-3M	0	106	106
3M-1YR	64	35	99
1YR-3YRS	81	14	95
TOTAL	145	155	300

DURATION OF STAY

AVERAGE DURATION OF STAY						
AGE-GROUP WISE & GROWTH & NON GROWTH						
	GROWTH		NON GROWTH		TOTAL	
		AVERAGE		AVERAGE		AVERAGE
1M-3M	589/38	15.5	713/67	10.6	1302/105	12.4
3M-1YR	357/24	14.8	787/76	10.5	1144/100	11.4
1YR-3YR	271/18	15	779/77	10.1	1050/95	11
TOTAL	1217/80	15.2	2279/220	10.4	3496/300	11.65

Overall,the average duration of stay was 11.65 days.The average duration of stay among culture positive cases was 15.2 days and among culture negative cases was 10.4 days.The longest duration of stay among the different age groups was in the 1-3 months category.

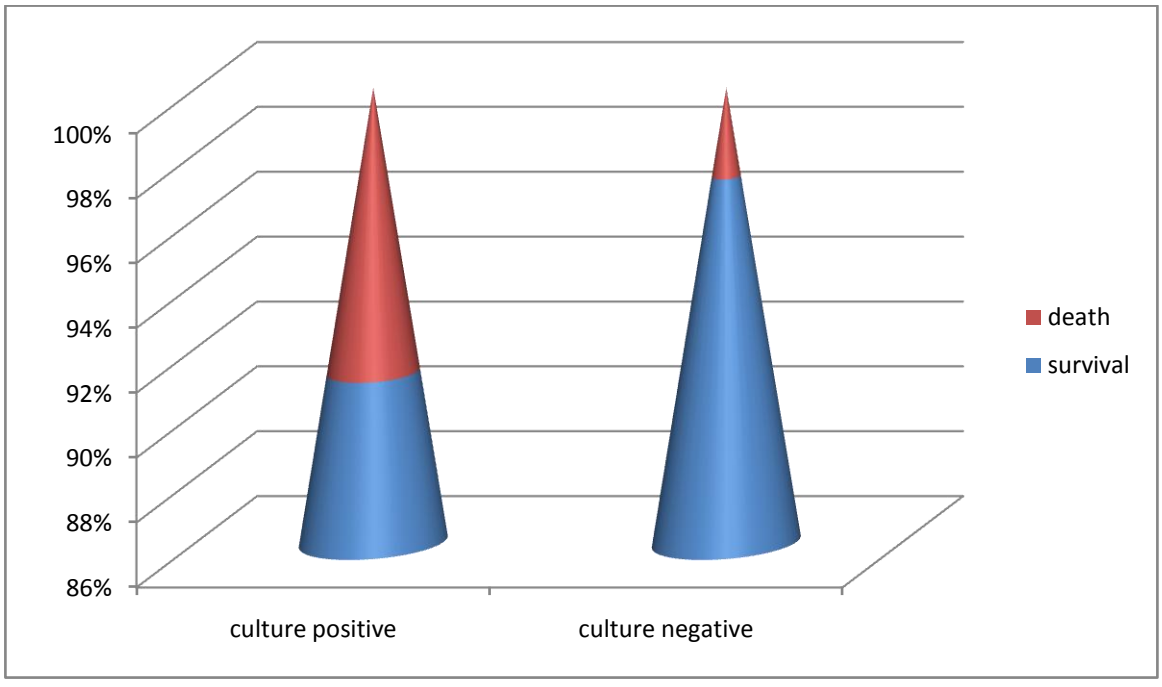


MORTALITY

DEATH			
AGE-GROUP	GROWTH	NON GROWTH	TOTAL
1M-3M	6	2	8
3M-1YR	1	4	5
1YR-3YR	0	0	0
TOTAL	7	6	13

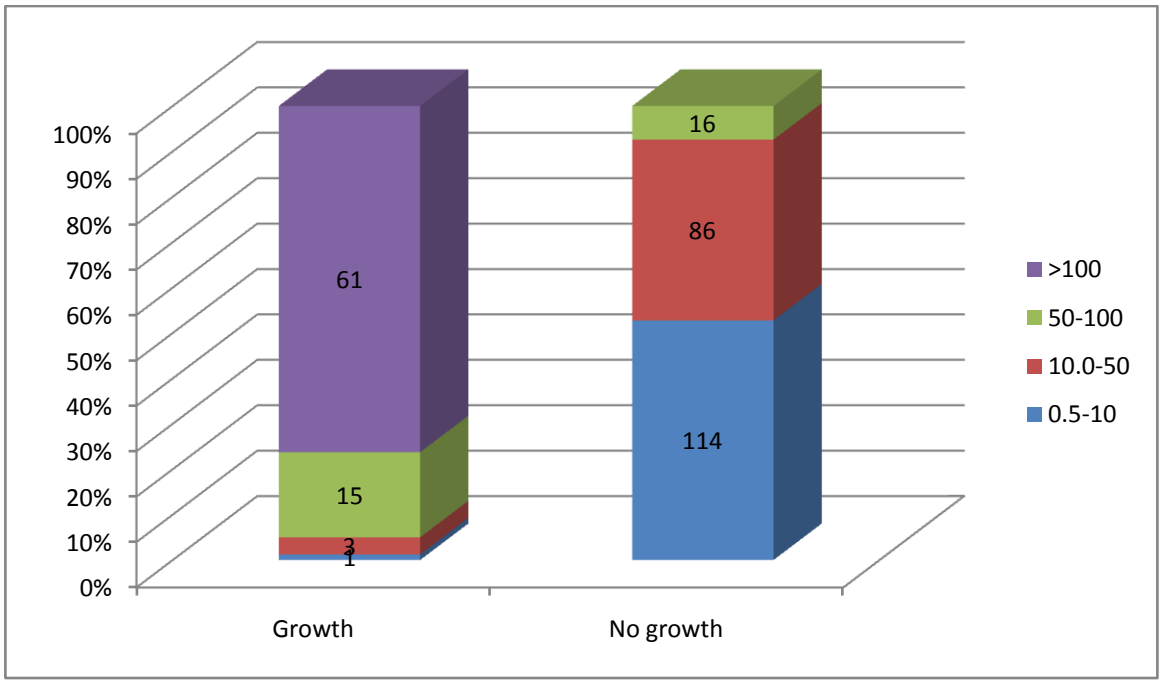
The overall mortality was 13 cases among the 300 (4.35%) of which 7 cases were among culture positive cases.These were all caused due to Staphylococcus aureus.

The mortality among culture positive cases was 8.75% and among culture negative cases was 2.7% (P<0.05) which was statistically significant.



COMPARISON OF PROCALCITONIN VALUES AMONG CULTURE POSTIVE AND CULTURE NEGATIVE CASES

PCT LEVELS(NG/ML)	GROWTH WISE - PCT		TOTAL
	GROWTH	NO-GROWTH	
0.5-10	1	114	115
10-50	3	86	89
50-100	15	16	31
>100	61	4	65
TOTAL	80	220	300



The levels of procalcitonin was highest in the culture positive cases when compared to culture negative cases.76.25% in the growers had PCT levels >100 where as in the culture negative cases PCT levels more than 100 was seen in only 7.27% of cases.(P<0.01) The difference of average PCT values amont the two groups was statistically significant.

ANTIBIOGRAM

As discussed earlier the most common organism isolated was staphylococcus aureus.Most of the isolates of S.Aureus (among isolated 46 growths) were sensitive to amikacin followed by teicoplanin and vancomycin.

Among the first line of antibiotics,amikacin is the antibiotic having

TABLE - 12		AMP	CLOX	OXA	CEFOT	CFZL	AK	GA	CIP	OFLO	COT	VAN	PIP	MER	TEI
PNEUMO	**R**	3	3	3	1	1	4	4	1	2	3	0	0	0	0
	S	1	1	1	3	3	0	0	2	2	1	4	4	4	4
STAPH	**R**	39	32	31	24	18	5	20	10	21	34	8	0	0	7
	S	7	14	15	22	28	41	26	36	25	12	38	0	0	39
EC	**R**	6	5	5	0	0	3	5	0	1	7	7	0	0	0
	S	3	4	4	9	9	6	4	9	8	2	2	9	9	0
KL	**R**	10	10	10	5	5	5	6	10	9	9	10	2	0	0
	S	2	2	2	7	7	7	6	2	3	3	2	10	12	0
ENT	**R**	3	2	2	4	4	4	5	3	3	3	1	2	2	0
	S	3	4	4	2	2	2	1	3	3	3	5	4	4	6
PS	**R**	2	2	2	1	1	2	0	2	2	2	2	2	0	0
	S	0	0	0	1	1	0	2	0	0	0	0	0	2	0
TOTAL	**R**	66	58	57	33	30	23	39	25	38	60	32	2	2	7
	S	13	21	22	46	49	56	40	54	41	19	47	29	29	41

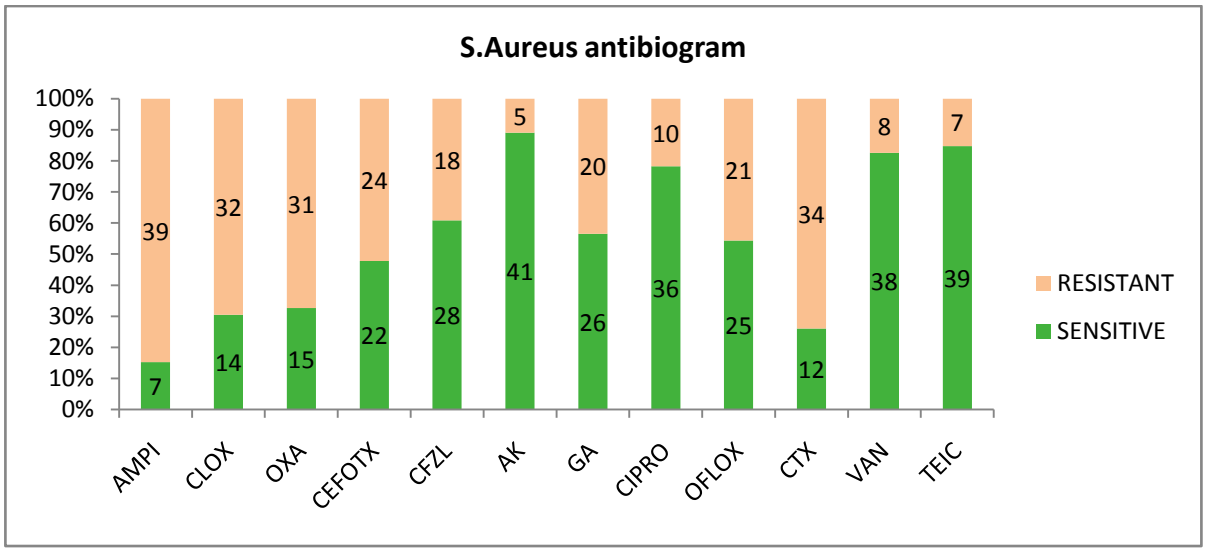
maximum sensitivity against all isolates(56/80=70% coverage

The second antibiotic with maximum action against all organism would be ciprofloxacin(54/80=67.5%)

The antibiogram and resistance patterns of each organism are discussed in detail

STAPHYLOCOCCUS AUREUS

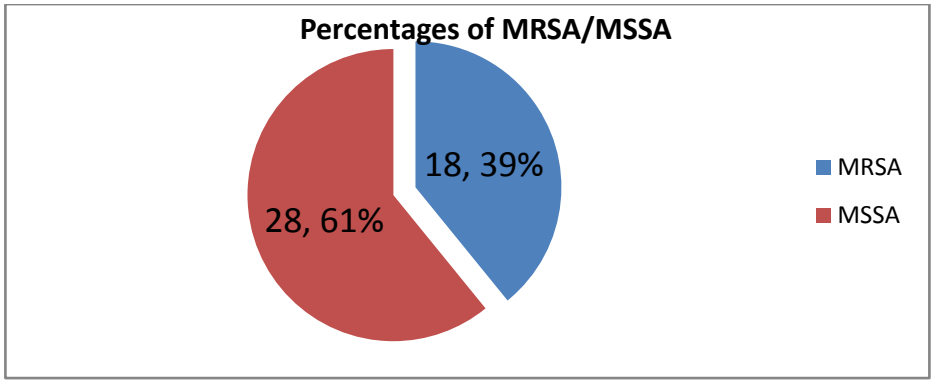
Among the 80 patients showing culture positivity ,46(57.5%) were S.Aureus



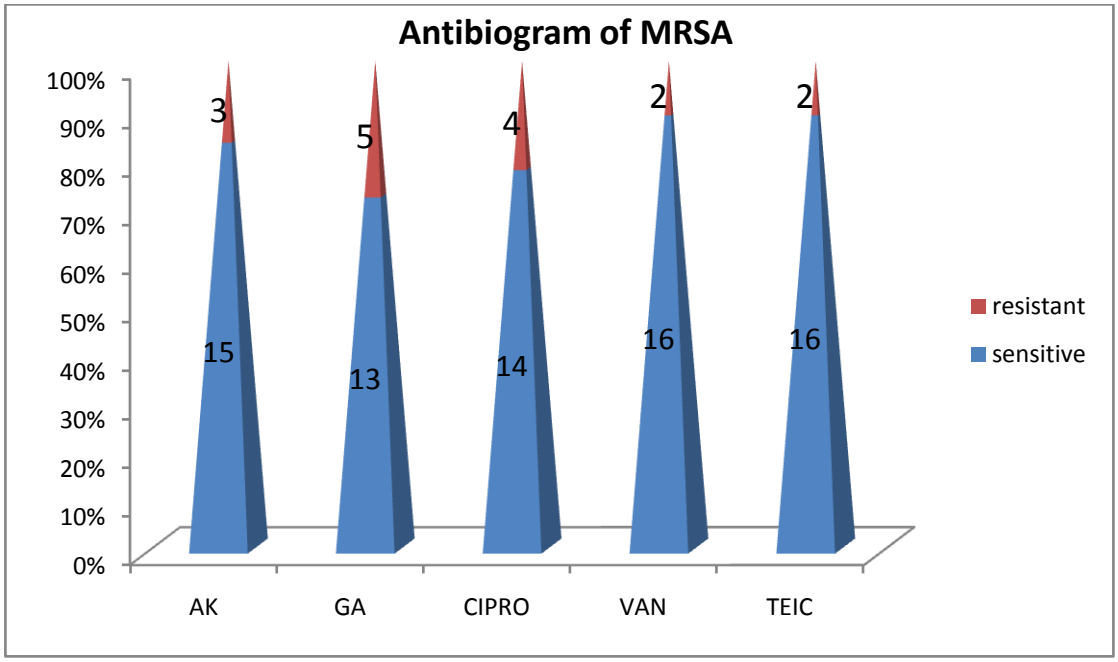
Among the first line agents ,amikacin had the maximum sensitivity covering 89%(41/46) of S.Aureus.

This was followed by ciprofloxacin-78.2%(36/46)

The percentage of MRSA was 39.1%(18 of 46) of the S.Aureus grown



Of the MRSA isolated 88.9% were sensitive to vancomycin followed by 83.3% sensitivity to amikacin



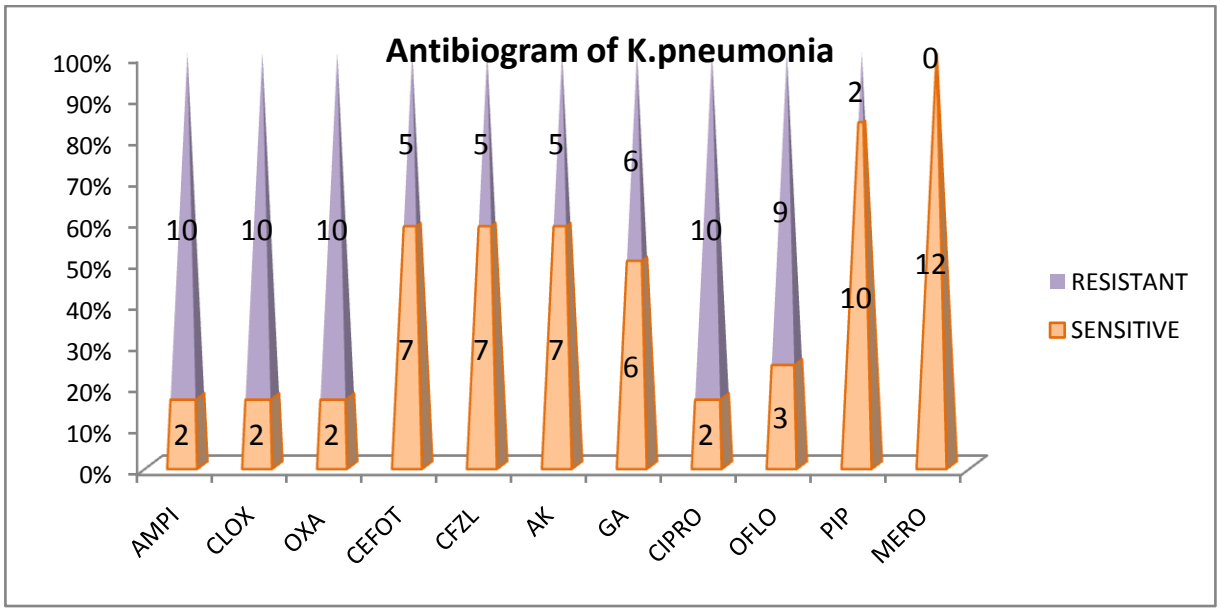
The percentage of overall resistance to vancomycin was 17.3% (8/36)and to teicoplanin was 15.2%.(7/46).

Two of the staphylococci were resistant to all the above mentioned drugs.

Further antibiotic sensitivity showed them to be sensitive to linezolid.

KLEBIELLA PNEUMONIAE

The second most common organism isolated overall was Klebsiella



Among the isolates maximum sensitivity was by meropenam.All isolates(100%) were sensitive to meropenam. I.e,no carbapenamase producing klebsiella were isolated.

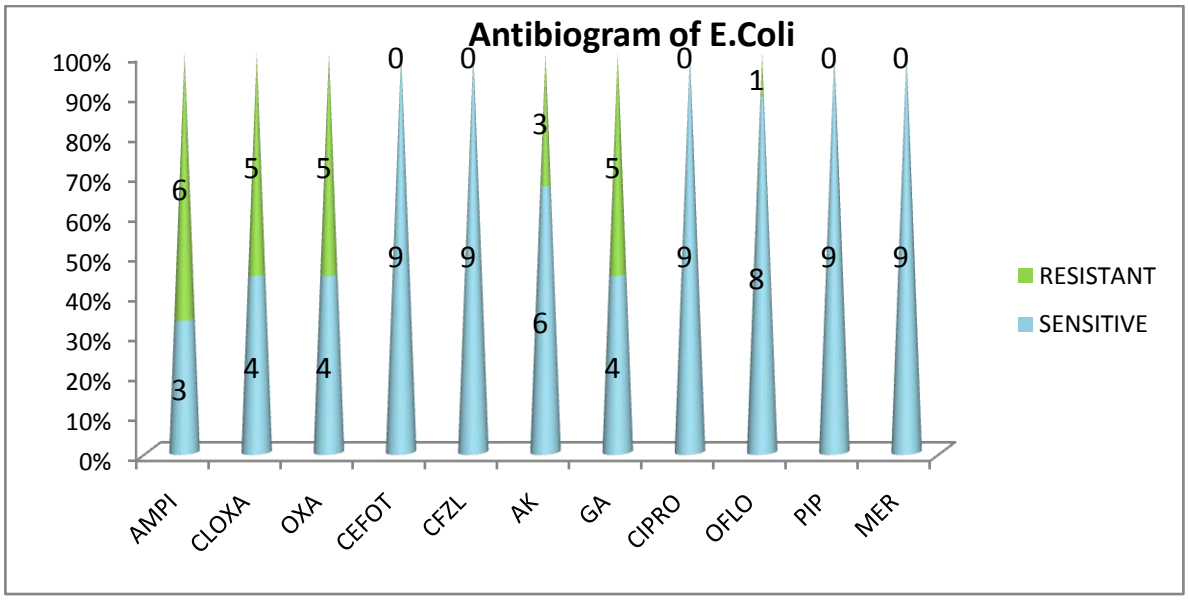
83.3% of isolates were sensitive to piperacillin and 58.33% of isolates were senstitive to amikacin.

Flouroquinolone sensitivity was only 16.6%(2 isolates).

The percentage of ESBL resistance was 16.67% i.e 2 isolates were resistant to penicillin and cephalosporin group of antibiotics.

ESCHERICHEA COLI

9(11.25%) of culture positive isolates were E.Coli



All the isolates were sensitive to cephalosporins,ciprofloxacin,piperacillin and meropenam.

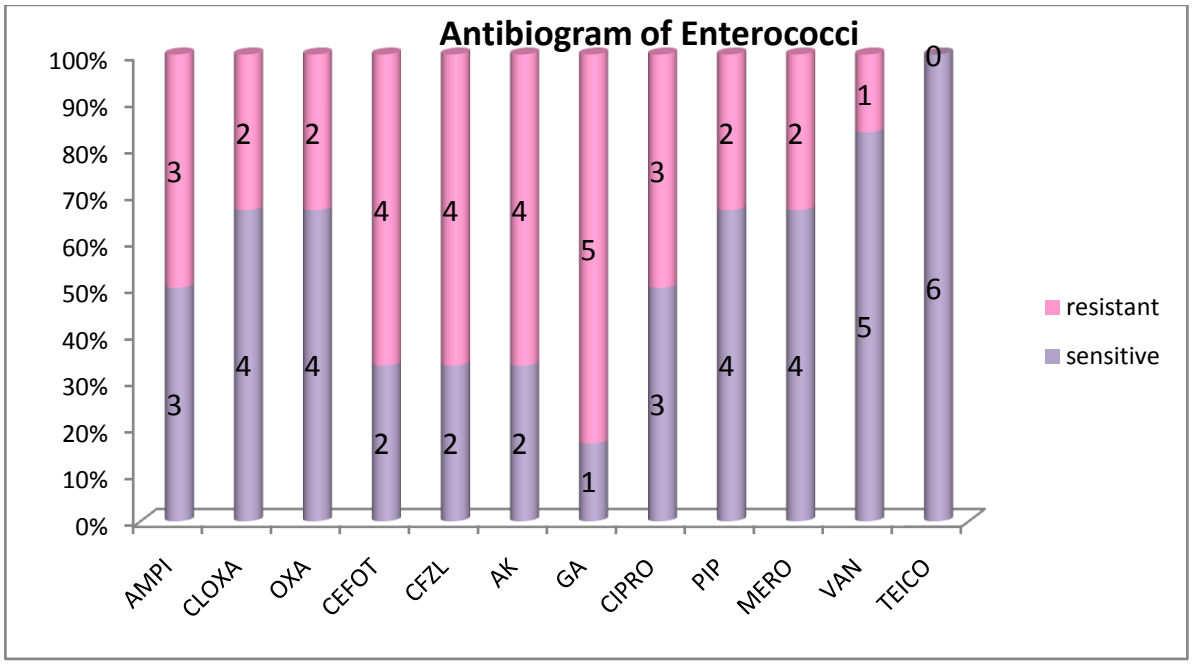
None of the isolates were ESBL producers.

Resistance to amikacin was seen in 33% (3/9) of isolates.

Ampicillin resistance was seen in 33% of isolates.

ENTEROCOCCI

Enterococci accounted for 7.5% of the total organisms grown i.e 6 out of 80 oraganisms.



Among penicillin group,50% were sensitive to ampicillin 3,33% sensitive to cloxacillin and oxacillin.

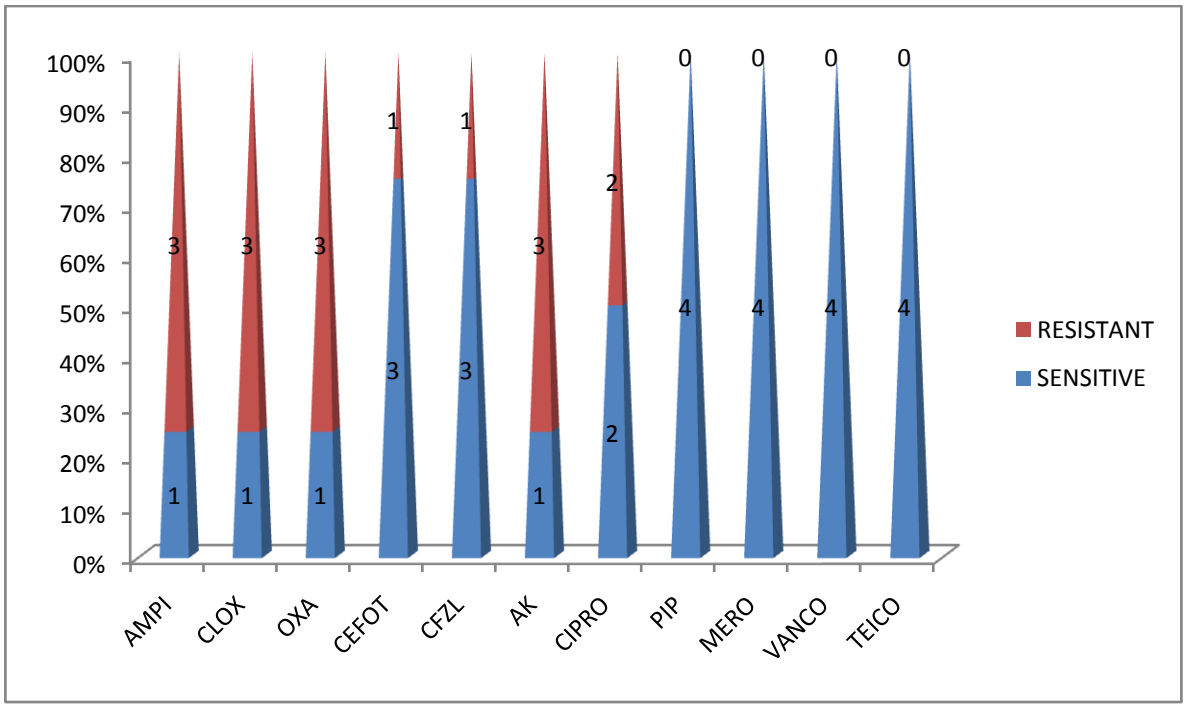
The enterococci shwed high degree of resistance to cephalosporins with 66.67% being resistant.

One of the isolate was vancomycin resistant-VRE(16.67%).

All the isolates were sensitive to teicoplanin.

STREPTOCOCCUS PNEUMONIAE

Of the organisms isolated pneumococci formed 5%(total of four organisms)



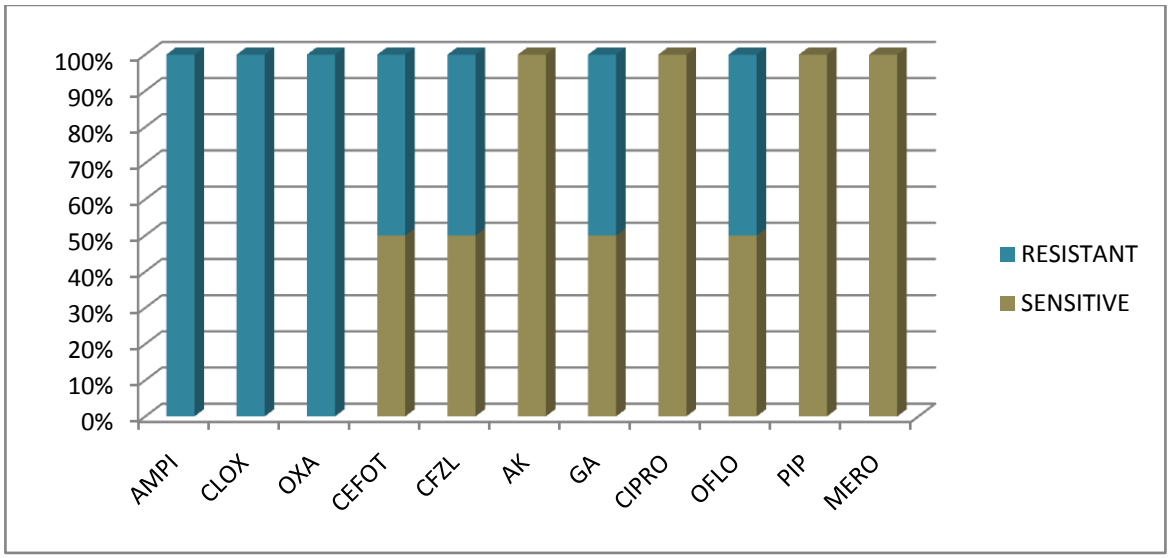
All isolates had 33% sensitivity to ampicillin,cloxacillin and oxacillin.

66% were sensitive to cephalosporins.

100% were sensitive to piperacillin,meropenam,vancomycin and teicoplanin.

PSEUDOMONAS AERUGINOSA

Two organisms were isolated and both were in immunocompromised patients(under chemotherapy) accounting to 2.5% of total growth.



All isolates were100% resistant to ampicillin,cloxacilli and oxacillin.

All were sensitive to piperacillin ,ciprofloxacin,amikacin and meropenam.

Among cephalosporins 50% resistance was observed

DISCUSSION

1.CULTURE POSITIVITY RATE:

In our study the percentage of positive blood cultures was 27 %(80 out of 300)..

In the study by Tiwari et al (Bangalore),the percentage of positive blood cultures was similar to our study -25%(32/128) which was similar to our study,this being an Indian study.

In similar studies done in Cambodia by Stoessor et al and in Kabul by Tariq et al the percentage of culture positivity was only 7.9% and 12.2% respectively.

The method and culture media used were not discussed in detail.

Our study was done using automated blood culture with inactivating agents for antibiotics which probably resulted in a higher yield.

2.ISOLATES

In our study the most common organism islated was S.Aureus accounting for 58.75% (46 isolates) followed by 12 Klebsiella(15%),E.coli(11.25%), Enterococci(7.5%)Pneumococci(5%) and Pseudomonas(2.5%)

In the various previous studies majority isolated were gram negative organisms in contrast to our study.In the sudy by Stoesser et al,Salmonella tpyhi was the most common organism isolated(22.8%) followed by Stahylococcus aureus.In study by Tiwari et al,the most common organism was Klebsiella(43%) followed by S.Aureus (18.75%).The study by Tariq et al shows that CONS was the most common isolate(26.34%) followed by klebsiella.Thus the most common organism varied among different studies with predominant gram negative organisms.The second most common organism in two of the above mentioned studies was S.Aureus which was the commonest organism isolated in our study.

3.ANTIBIOGRAM

In our study the antibiotic covering most isolates was amikacin (89%) followed by ciprofloxacin(78%)

Of the staphylococci 39% were MRSA in our study compared to 79% in the study by Sabouri et al,50% in the study by Tamma et al .In the study by Tiwari et al at Bangalore the % of MRSA was similar to in our study i.e.33.33%

Among the gram negative isolates 51.9% produced ESBL in the study by Tamma et al .In our study EBBL production was 16.7%.The low levels of

resistance among the gram negative organisms in our study may be due to the isolates being community acquired and more from medical wards rather than ICU settings where a high degree of resistance would be seen.

Most of the gram negative organisms were showing increasing resistance to b-lactam antibiotics and most of the staphylococci worldwide are resistant to penicillin

LIMITATIONS

Though our study included a large number of patients,group stratification based on the foci was not done in view of various difficulties.Further they represent only the cases referred to tertiary care centre limiting its application to all centres.The differences among immunocompromised and immunocompetant patients was not comsidered.Also cases were taken only from medical wards and surgical cases were not considered.Anaerobic organisms were not considered as they contribute little to pediatric sepsis.The percentage of cases from ICU settings was less compared to other studies which may account for the lower mortality of sepsis in our study.

CONCLUSION

INTERPRETATION AND CONCLUSIONS

There is an shift of organisms grown from the gram negative to gram positive spectrum,with the most common organism being Staphlycoccus aureus.(58%) None of the isolates were H.Influenza meaning increasing immunization coverage(74%) against them decreasing their incidence.

The prevalence of MRSA is high(39%).There is also increasing resistance to b-lactam antibiotics among all gram positive isolates and ESBL production among klebsiella.(16.67%)This increases the hospital stay and more monetary wastage for the higher antibiotics used and higher toxicity.

SUMMARY

This study was conducted in the institute of child health and hospital for children,Chennai with the aim of isolating and identifying bacterial etiological agents responsible for sepsis in children aged 1-36 months and determining the susceptibility patterns of isolates .

300 Children admitted in ICH &HC fulfilling the inclusion criteria were included in the study.

Informed consent obtained from parents

Blood was collected in BHI broth for initial culture by automated blood culture(bacT/ALERT PF) and subcultures were done based on isolates.

Antibiotic susceptibility of the isolates were determined.

The percentage of culture positivity was 27%(80/300).

Staphlococcus aureus was the most common organism isolated accounting for 58.75% of overall isolates.The next most common being klebsiella.(15%)

Among the first line agents ,amikacin had the maximum sensitivity covering 89%(41/46) of S.Aureus.This was followed by ciprofloxacin-78.2%(36/46)

The percentage of MRSA of the Staph isolates was 39.1%.The percentage of VRSA was 17.3%.

Among klebsiella ESBL production was 16.67% and all were sensitive to meropenam.

Enterococci showed high degree of resistance to cephalosporins(61.6%).VRE(Vancomycin resistant enterococci) acoounted for 16.67%.

Among all isolates ,the antibiotic with maximum coverage was amikacin (70%) followed by ciprofloxacin(67.5%).

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ABBREVIATIONS

SIRS-Systemic inflammatory response syndrome

MODS-Multi Organ Dysfunction Syndrome

TLR-Toll Like Receptors

PAMP-Pathogen Assosiated Molecular Pattern

VEGF-Vascular Endothelial Growth Factor

TNF-a-Tumor Necrosis Factor alpha

CRP-C-Reactive protein

PCT-Procalcitonin

eNOS –epithelial derived Nitric Oxide Synthase

BNP-Brain natriuretic peptide

NT-BNP-Amino Terminal BNP

AMR-Antimicrobial resistance

WHO-World Health Organisation

MIC-Minimum Inhibitory Concentration

ESBL-Extended Spectrum B-Lactamase

MRSA-Methicillin resistant Staphylococcus aureus

VRSA-Vancomycin resistant Staphylococcus aureus

NTS-Non typable salmonella

VRE-Vancomycin resistant Enterococci

MICROBES AND ANTIBIOTICS IN TABLES

PNEUMO-pneumococci

STAPH-Staphylococcus aureus

EC-Escherichea coli

KL-Klebsiella pneumonia

PSEUDO-Pseudomonas aeruginosa

ENTERO-Enterococci

AMPI-Ampicillin

OXA-Oxacillin

CLOX-Cloxacillin

CEFOTX-Cefotaxime

CFZL-Cefazolin

AK-Amikacin

GA-Gentamycin

CIPRO-Ciprofloxacin

OFLO-Ofloxacin

VAN-Vancomycin

PIP-Piperacillin

MERO-Meropenam

TEICO-Teicoplanin

CONSENT FORM

ஆராய்ச்சி ஒப்புதல் படிவம்

என் குழந்தைக்கு காய்ச்சல் அதிகமாக இருப்பதால் இரத்தத்தில் பாக்டீரியா கிருமி இருக்கும் வாய்ப்பு அதிகம் என்பதை அறிந்துகொண்டேன்.

இரத்தத்தில் பாக்டீரியா கிருமி இருந்தால் அதனால் பல்வேறு உறுப்புகளுக்கு பரவும் வாய்ப்பு அதிகம் என்பதையும் அறிந்துகொண்டேன்.

சரியான நேரத்தில் அக்கிருமியை கண்டறிந்து தக்க மருந்து (ஆண்டிபயாட்டிக்) கொடுக்கப்பட்டால் கிருமி பரவும் வாய்ப்பு குறைந்து குழந்தை சீக்கிரம் குணமடைய வாய்ப்புள்ளது என்பதை அறிந்துகொண்டேன்.

எனவே **'இரத்தத்தில் பாக்டீரியா தன்மை கண்டறிதல் மற்றும் அது கட்டுப்படும் ஆண்டிபயாடிக்கின் எதிர்ப்புத்தன்மை கண்டறிதல்'** எனும் ஆராய்ச்சியில் என் குழந்தைக்கு இரத்தம் (1மி.லி அளவு) எடுத்து பரிசோதனை செய்து கொள்ள எவ்வித நிர்பந்தமும் இன்றி சம்மதிக்கிறேன்.

இந்த பரிசோதனை என் குழந்தைக்கு இன்றியமையாத ஒன்று என்பதை அறிந்துகொண்டேன்.

இது மிக எளிய பரிசோதனை என்றும் பாதிப்புகள் மிகக் குறைவு (சிறிய அளவு இரத்தக்கசிவு) என்றும் அறிந்துகொண்டேன்.

எனவே என் குழந்தை இவ்வாராய்ச்சியில் பங்கேற்க முழு சம்மதத்தை தெரிவிக்கிறேன்.

பெற்றோர் கையொப்பம்
பெயர் சாட்சி-1

இடம் :
தேதி : சாட்சி-2

ஆராய்ச்சியாளர் கையொப்பம்

INFORMED CONSENT FORM

As my child has high grade fever. I have been informed that the probability of sepsis (Blood born infection with bacteria) is high in my child.

I have been informed regarding the complications of sepsis and its effect on various organs.

I have been told the need of identifying the bacteria early and the antibiotics which the bacteria are susceptible to as my child may recover faster with appropriate antibiotics.

Hence, I give my consent for obtaining 1ml of blood from my child in view of participating in this research of 'Bacterial etiological agents of sepsis and its antibiotics sensitivity pattern'. I give my consent with full knowledge without any external force influencing me.

I realise that this test is indispensable for my child.

Hence I give my full consent for my child to participate.

Parent's Signature
(Name)

Witness-1

Place :
Date :

Witness-2

Researcher's Signature

PATIENT DATE FORM

Age

Gender

Place

Socioeconomic status

Duration of fever

Assosiated symptoms

Previous hospitalisation and duration

Prior antibiotics and duration(past two weeks)

Immunosuppresion*

Immunisation(pneumococcal,Hib)

Peak temperature

Total counts

CRP

PCT

CXR

Focus*

Grams stain

Culture isolate

Antibiotic susceptibility

Emperical antibiotic

Breast feeding

Duration of stay

Outcome

NAME	AGE	IP NO	SEX	SOCIOECONOMIC STATUS	BREAST FEEDING	IMMUNISATION	DURATION OF STAY	OUTCOME	TC	CRP	PCT	NEC	ORGANISI	AMPI	CLOX	OXA	CEFTX	CEFAZ	AK	GA	CIPRO	OFLO	COT	VAN	PIP	MER	TEI
GOWTHAI	1	804045	M	5	N	N	10	C	2	P	4	G	PNEUMO	R	R	R	S	S	R	R	S	S	R	S	S	S	
GOPI	2	804755	M	3	Y	Y	8	C	1	P	1	NG															
SARAVAN	3	804762	M	4	Y	Y	7	C	2	P	2	NG															
DEEPIKA	2	806166	F	3	Y	N	9	C	2	P	1	NG															
DAVID	1	806165	M	5	Y	N	21	D	1	P	4	G	STAPH	R	R	R	R	R	S	R	S	S	R	R			R
DIVYASUG	3	806302	F	4	N	N	15	C	1	P	3	G	STAPH	R	R	S	S	S	S	R	S	R	R	R			S
CHRISTIN/	2	806456	F	3	Y	Y	7	C	2	P	2	NG															
VELMURU	2	806475	M	5	Y	N	4	D	1	P	2	NG															
SURESH	1	806465	M	3	Y	N	10	C	2	P	1	NG															
YAASINI	2	806988	F	4	Y	N	15	C	2	P	3	G	STAPH	R	R	R	S	R	S	S	S	S	S	S			S
ILAVARAS	1	807061	F	5	Y	N	15	C	1	P	4	G	STAPH	R	R	R	S	S	S	S	S	R	R	R			R
SATHISH	1	807065	M	3	Y	N	14	C	2	P	3	G	EC	S	S	S	S	S	S	S	S	S	S	S			S
SHOBANA	2	807073	F	4	Y	Y	8	C	2	P	1	NG															
KAMALAK	1	807071	M	5	N	N	21	C	1	P	4	G	STAPH	R	R	R	R	R	S	R	S	R	R	S			S
SHARUN	1	807200	M	4	Y	N	10	C	1	P	1	NG															
DIWAKAR	2	807183	M	5	N	N	15	C	2	P	4	G	STAPH	R	R	R	S	S	S	R	S	R	R	R			S
DIVYASRE	3	807916	F	4	Y	Y	11	C	2	P	2	NG															
HARISH	2	807892	M	3	N	Y	8	C	2	P	1	NG															
HEMANTH	3	807806	M	4	N	N	14	C	1	P	3	G	KL	R	R	R	S	S	S	S	S	S	R	R	S	S	
MADAN	3	807823	M	3	Y	Y	10	C	2	P	2	NG															
SANJANA	2	808612	F	4	N	N	7	C	2	P	2	NG															
GOKUL	2	808141	M	3	Y	Y	8	C	2	P	1	NG															
ADITYA	3	808120	M	5	N	N	16	C	2	P	3	G	ENT	S	S	S	S	S	S	S	S	S	S	S			S
MONISHA	3	808215	F	3	Y	Y	9	C	2	P	2	NG															
LAKSHMI	2	806240	F	4	Y	Y	13	C	2	P	1	NG															
ALAN	1	808603	M	5	Y	N	16	D	1	P	4	G	EC	R	R	R	S	S	S	S	S	S	S	S	S	S	
DIVYA	3	809063	F	3	Y	Y	8	C	2	P	2	NG															
SIVARASH	2	808874	F	3	Y	Y	10	C	2	P	2	NG															
SANJAY	3	809276	M	4	Y	Y	8	C	2	P	1	NG															
AKASH	2	807333	M	4	Y	Y	12	C	2	P	2	NG															
PRIYA	1	809459	F	5	N	N	16	C	1	P	4	G	KL	S	S	S	S	S	S	S	S	S	S	S	S	S	
PORSELVI	3	809472	F	3	Y	N	11	C	2	P	2	NG															
PARGAVI	2	809464	F	4	Y	Y	16	C	2	P	1	NG															
RITHISH	2	809512	M	5	N	N	17	C	2	P	4	G	STAPH	R	R	R	R	R	R	R	S	S	R	S			S
VETRIVEL	3	805969	M	3	Y	Y	8	C	2	P	2	NG															
PRINCE	1	809599	M	4	N	Y	10	C	2	P	1	NG															
DILLIBABU	2	809605	M	4	N	N	17	C	1	P	3	G	EC	R	R	R	S	S	S	S	S	S	R	R	S	S	
PRAVEEN	3	810230	M	4	Y	Y	8	C	2	P	2	NG															
YASHWAN	1	810256	M	3	N	N	9	C	2	P	1	NG															
SURYA	2	810371	M	5	Y	N	7	C	2	P	1	NG															
GOKULRA	1	810205	M	5	N	N	16	D	1	P	4	G	STAPH	R	R	R	R	R	S	S	S	R	R	R			R
SWETHA	3	810200	F	3	Y	Y	10	C	2	P	2	NG															
DHARSHA	2	810282	M	4	N	N	16	C	2	P	3	G	EC	R	R	R	S	S	S	S	S	S	R	R	S	S	
BHUVANE	1	810322	M	3	Y	N	11	C	2	P	1	NG															
DHANUSR	1	810404	F	4	Y	N	14	C	2	P	4	G	STAPH	R	R	R	R	R	S	R	R	R	R	S			S
DHANUSH	3	810407	F	4	Y	Y	11	C	2	P	2	NG															
KEERTHIK/	2	810448	F	3	Y	Y	12	C	2	P	1	NG															
SIVASANK	1	810458	F	3	Y	N	13	C	1	P	2	NG															
SANTHOSI	2	812335	M	3	Y	Y	8	C	2	P	2	NG															
MONISH	1	812414	M	4	N	N	15	C	1	P	4	G	KL	R	R	R	R	R	R	R	S	S	R	R	S	S	
KEERTHIK/	3	812496	F	3	Y	Y	11	C	2	P	2	NG															
NIRUPAM	2	812495	M	3	Y	N	9	C	2	P	1	NG															
JENANI	1	812793	F	3	Y	N	8	C	1	P	1	NG															
B/O CHITR	1	813223	F	5	Y	N	17	D	1	P	4	G	ENT	R	R	R	R	R	R	R	R	R	R	R	R	R	
B/O SANJ/	1	813254	F	5	Y	N	14	C	1	P	3	NG															
JEYENDAR	2	813783	M	3	Y	Y	15	C	2	P	1	NG															
NAREN	3	813777	M	3	Y	Y	8	C	2	P	2	NG															
JAGADEES	3	813912	M	5	N	N	17	C	2	P	2	G	PS	R	R	R	R	R	R	R	S	R	R	R	S	S	
KIRTHIK	2	813931	M	4	Y	N	11	C	2	P	2	NG															
SHEWTHA	3	813997	F	4	N	N	12	C	1	P	3	G	STAPH	S	S	S	S	S	S	S	S	S	S	S			S
VIGNESH	2	814361	M	5	N	N	12	C	2	P	4	G	STAPH	R	S	S	S	S	S	S	S	S	R	S			S
APPU	1	814350	M	5	N	N	14	C	1	P	4	G	STAPH	R	R	R	R	R	S	R	R	R	R	S			S
KARTHIK	3	814582	M	3	Y	Y	8	C	2	P	2	NG															
SHALINI	2	814662	F	4	Y	Y	9	C	2	P	1	NG															
SHANMAT	1	814613	F	3	N	N	8	C	2	P	1	NG															
LOKESHW	3	814649	F	3	Y	Y	9	C	2	P	2	NG															
TEJESHWA	3	815305	F	3	Y	Y	9	C	2	P	1	NG															
VETRIVEL	1	815747	M	5	N	N	14	D	1	P	4	NG															
DIWAKAR	2	815698	M	4	N	N	16	D	2	P	3	NG															
JEYACHAN	2	815758	M	4	N	N	14	C	2	P	4	G	KL	R	R	R	S	S	S	S	S	S	R	R	S	S	
VIMALESH	1	815764	M	5	Y	N	17	C	2	P	3	G	STAPH	R	R	R	S	S	S	S	S	R	R	S			R
ASMI	3	816160	F	3	Y	Y	11	C	2	P	2	NG															
LAKSHMI	2	816162	F	3	Y	Y	13	C	2	P	2	NG															
GANESH	1	816172	M	3	N	N	15	C	2	P	2	NG															
VETRI	2	815766	M	4	Y	Y	9	C	2	P	1	NG															
DIWAKAR	3	815699	M	5	Y	Y	10	C	2	P	3	NG															
JAGADEES	1	816400	M	5	N	N	16	C	2	P	4	G	PNEUMO	R	R	R	S	S	R	R	S	R	R	S	S	S	
HARSHIKA	2	816399	F	4	Y	Y	11	C	2	P	2	NG															
YOSHITHA	3	816428	F	4	Y	Y	12	C	2	P	1	NG															
PREETHI	2	817029	F	5	N	N	16	C	2	P	4	G	STAPH	R	R	R	S	S	S	R	S	S	R	S			S
OVIYA	1	817004	F	3	Y	N	11	C	2	P	3	NG															
SRUTHIKA	2	817006	F	3	Y	Y	12	C	1	P	2	NG															
PREETHIK/	3	817038	F	4	Y	Y	13	C	2	P	2	NG															
PRIYADHA	1	817685	F	5	Y	N	17	C	1	P	4	G	EC	R	R	R	S	S	S	R	S	R	R	R	S	S	
LOGESHW	3	817682	M	3	Y	Y	8	C	2	P	2	NG															
LAKSHITH/	2	817782	F	4	Y	N	9	C	2	P	1	NG															
SAFI	1	818840	M	3	Y	N	7	C	2	P	1	NG															
VIGNESHV	3	818903	M	3	Y	Y	9	C	2	P	1	NG															
VIJAY	3	818897	M	5	N	N	18	C	2	P	4	G	KL	R	R	R	R	R	R	R	R	R	R	R	S	S	
JAGADESH	1	818973	M	5	N	N	16	C	2	P	3	G	STAPH	S	S	S	S	S	S	R	S	S	R	S			S
THIRUMAL	3	819012	M	3	Y	Y	11	C	2	P	1	NG															
LOKESH	2	818977	M	4	Y	Y	12	C	2	P	1	NG															
PURUSOTI	1	818983	M	3	N	N	12	C	2	P	1	NG															
JABIN	1	819444	M	5	Y	N	15	C	1	P	4	G	STAPH	R	R	R	R	R	R	R	S	R	R	S			S
JAGADEES	2	819462	M	4	N	N	16	C	2	P	4	G	ENT	R	R	R	S	S	R	R	R	R	R	R	S	S	
SANTHOSI	3	819820	M	3	Y	Y	9	C	2	P	2	NG															
NANDITA	1	819730	F	3	Y	N	8	C	2	P	1	NG															
LAKSHMI	3	820245	F	3	Y	Y	8	C	2	P	2	NG															
SHOBIKA	2	820299	F	3	Y	N	9	C	2	P	1	NG															
VIGNESH	2	820268	M	3	Y	N	11	C	2	P	1	NG															
PRIYADHA	2	820322	F	3	Y	Y	12	C	2	P	2	NG															
LAKSHMI	1	820647	F	4	N	N	13	C	2	P	4	G	PNEUMO	R	R	R	S	R	R	R	S	S	R	R	S	S	
GOWTHAI	2	820644	M	5	N	Y	15	C	1	P	4	G	STAPH	R	S	S	S	S	S	R	S	R	R	S			R
PRADDEPI	3	820637	M	3	Y	Y	14	C	2	P	2	NG															
GOKUL	1	820679	M	4	Y	N	8	C	1	P	1	NG															
AMLU	2	820717	F	5	N	Y	9	C	2	P	1	NG															
KAVIYARA	3	820782	M	3	Y	Y	7	C	2	P	2	NG															
HARIKRISI	1	820865	M	5	N	N	16	C	1	P	4	G															
AJAY	2	820853	M	3	Y	N	12	C	2	P	2	NG															
ASHIKA	3	820857	F	3	Y	Y	11	C	2	P	1	NG															
JAYASURIY	2	820935	M	5	N	N	16	C	2	P	4	G	PNEUMO	R	R	R	S	S	S	S	S	S	S	R	S	S	
KAMESHW	3	820906	M	3	Y	Y	13	C	2	P	2	NG															
SANDHYA	1	820996	F	3	Y	N	14	C	2	P	1	NG															
AARTHI	2	820712	F	4	Y	Y	15	C	2	P	2	NG															
RASHIKA	3	821062	F	5	N	Y	16	C	2	P	4	G	STAPH	R	R	R	R	S	S	S	S	S	R	S			S
SAIBALAJI	1	821060	M	3	Y	N	11	C	2	P	1	NG															
ANJALAI	2	821051	F	4	N	Y	15	C	2	P	4	G	STAPH	R	R	R	R	R	S	S	R	R	R	S			S
KISHORE	3	821032	M	3	Y	N	10	C	2	P	2	NG															
THIRUVAS	1	821117	M	5	N	Y	15	C	2	P	4	G	STAPH	R	R	R	R	S	S	S	S	S	S	S			S
NISHA	2	821142	F	3	Y	Y	9	C	2	P	3	NG															
LAKSHITH/	3	821198	F	3	Y	Y	11	C	2	P	2	NG															
KAVIYA	1	821242	F	3	Y	N	12	C	1	P	1	NG															
ROSHINI	2	821211	F	3	Y	Y	10	C	2	P	2	NG															
SHEIKDAV	1	821327	M	4	Y	N	15	C	2	P	4	G	STAPH	R	R	R	S	S	S	S	S	R	R	S			S
PRAGADEI	2	821353	M	5	N	Y	16	C	1	P	3	G	STAPH	R	R	R	R	R	S	R	R	S	R	R			R
SUKUMAR	3	821321	M	3	Y	Y	9	C	2	P	1	NG															
SRINATH	1	821320	M	3	Y	N	8	C	2	P	1	NG															
THARUNK	2	821565	M	3	Y	Y	9	C	2	P	1	NG															
PRANAV	3	818125	M	3	Y	Y	9	C	2	P	2	NG															
JERIN	1	821612	M	3	Y	N	8	C	1	P	1	NG															
SIVAPRAK	2	821736	M	3	Y	Y	7	C	1	P	1	NG															
GOPIKRISI	3	821818	M	3	Y	Y	10	C	2	P	1	NG															
SURYA	1	821817	M	3	Y	N	11	C	2	P	2	NG															
MONISHA	2	821923	M	3	Y	Y	12	C	2	P	1	NG															
LINGESHW	3	821903	M	3	Y	Y	9	C	2	P	2	NG															
B/O DIVY/	1	821915	F	4	Y	N	16	D	1	P	4	G	EC	S	S	S	S	S	S	R	S	S	R	R	S	S	
AYESHA	3	821882	F	3	Y	Y	11	C	2	P	2	NG															
HARIKRISI	1	820865	M	3	Y	N	12	C	1	P	1	NG															
UDAYASH/	2	822370	M	3	Y	Y	13	C	2	P	1	NG															
MD SUJITH	3	822398	M	4	Y	Y	9	C	2	P	1	NG															
REENA	1	822396	F	5	N	N	17	C	2	P	4	G	KL	R	R	R	R	R	R	R	S	S	R	R	S	S	
DHARSHIN	2	822356	F	4	Y	Y	7	C	1	P	2	NG															
RITHISH	3	822413	M	3	Y	Y	8	C	1	P	3	NG															
RAJKUMA	3	822911	M	3	Y	N	15	C	1	P	2	NG															
KARTHIK	1	823139	M	3	Y	N	11	C	2	P	1	NG															
SAKTHIVE	2	823123	M	3	Y	Y	12	C	2	P	1	NG															
DHANAM	3	823036	F	5	Y	Y	16	C	1	P	4	G	STAPH	R	S	S	R	R	S	S	S	S	S	S			S
AKBAR AL	1	823028	M	4	Y	N	9	C	1	P	2	NG															
MAXON	1	823647	M	3	Y	N	8	C	2	P	2	NG															
SIVAPRAK	2	823642	M	3	Y	N	9	C	2	P	1	NG															
CHEZHIYA	3	823440	M	3	Y	Y	7	C	2	P	1	NG															
KABILESH	3	823929	M	5	N	Y	14	C	1	P	4	G	STAPH	R	R	R	S	S	S	R	S	S	R	S			S
RISHIBAL/	1	823931	M	5	N	N	15	C	1	P	4	G	STAPH	S	S	S	S	S	S	S	S	S	S	S			S
ABHILESH	2	823924	M	4	Y	Y	16	C	2	P	4	G	ENT	R	R	R	S	R	R	R	S	S	R	S	S	S	
ATHISH	3	823996	M	3	N	Y	9	C	1	P	3	NG															
DIVYADH/	1	823992	F	3	Y	N	9	C	2	P	2	NG															
GIRIRUDH	1	823994	M	3	Y	N	8	C	1	P	1	NG															
DHARMAD	1	824213	M	3	Y	N	7	C	1	P	1	NG															
CHAITANY	2	824358	M	3	Y	Y	9	C	2	P	1	NG															
SOLOMON	3	821287	M	3	Y	Y	10	C	2	P	1	NG															
SAM	3	824376	M	3	Y	Y	11	C	2	P	2	NG															
MADHAN	3	824326	M	3	Y	Y	8	C	2	P	1	NG															
EBENEZER	1	825256	M	4	Y	N	9	C	1	P	1	NG															
BHAVASRI	2	825267	F	3	Y	N	9	C	1	P	1	NG															
SRINISHA	3	825672	F	3	Y	Y	10	C	2	P	1	NG															
SANJAI	1	825673	M	3	N	N	11	C	1	P	1	NG															
DEVA	2	825861	M	3	Y	Y	12	C	2	P	2	NG															
NAVYASH	3	825913	F	5	N	Y	16	C	2	P	4	G	STAPH	R	S	S	S	S	R	R	S	S	R	S			S
NIRANJAN	3	825702	M	3	Y	Y	9	C	2	P	1	NG															
VIKASH	1	825558	M	3	Y	N	8	C	1	P	2	G	STAPH	R	R	R	R	S	R	R	S	R	R	S			S
B/O NEHA	1	825805	M	5	Y	N	15	C	1	P	4	NG															
THARUN	3	825605	M	3	Y	Y	8	C	2	P	2	NG															
DHARSHA	1	826151	M	3	Y	N	9	C	1	P	1	NG															
BEULAH	2	826578	F	3	Y	Y	12	C	2	P	1	NG															
B/O NAGA	1	826598	F	5	N	N	16	C	2	P	4	G	EC	S	S	S	S	S	R	R	S	S	R	R	S	S	
DHARSHIN	1	827137	F	3	Y	N	9	C	1	P	2	NG															
RANI	3	827120	F	3	Y	Y	8	C	2	P	1	NG															
HARIHAR/	1	827063	M	3	Y	N	9	C	2	P	1	NG															
NISHANTH	2	825015	M	3	Y	Y	10	C	2	P	1	NG															
BHUVANE	3	827129	M	3	Y	Y	11	C	2	P	1	NG															
MAHIDAS	1	827106	M	3	Y	N	12	C	2	P	1	NG															
B/O RAJES	1	828573	F	5	Y	N	16	C	1	P	4	G	STAPH	R	R	R	R	R	S	S	R	R	R	S			S
B/O VASA	1	828635	M	5	Y	N	17	C	1	P	4	G	STAPH	R	R	R	R	R	S	S	R	R	R	S			S
SANJAI	2	829161	M	3	Y	Y	8	C	2	P	1	NG															
DHARNIK/	3	829162	F	3	Y	Y	9	C	2	P	1	NG															
NANDHU	2	829111	F	3	Y	Y	10	C	2	P	2	NG															
TAMILISAI	3	829176	F	3	Y	Y	9	C	2	P	1	NG															
BHOOPAT	1	828813	M	4	Y	N	11	C	2	P	1	NG															
SANDHYA	2	829530	F	3	Y	Y	12	C	2	P	2	NG															
ASHWINI	3	829549	F	3	N	Y	13	C	2	P	1	NG															
SUDHARSI	1	828186	M	4	Y	N	10	C	2	P	1	NG															
DEEPANR/	3	829342	M	5	Y	Y	11	C	2	P	4	G	EC	R	S	S	S	S	R	R	S	S	R	R	S	S	
POOVARA	1	829245	M	4	Y	N	12	C	1	P	1	NG															
KAVISRI	2	829242	F	3	N	Y	14	C	2	P	4	G	KL	R	R	R	S	S	S	S	S	S	S	R	S	S	
KAMALI	3	829259	F	5	N	N	15	C	1	P	2	NG															
SANTHOSI	1	824566	M	4	Y	N	15	C	2	P	1	G	STAPH	R	R	S	R	S	R	S	S	S	R	S			S
VISNU	1	824535	M	3	Y	N	16	C	2	P	1	NG															
SUDEESH	3	830841	M	3	Y	Y	14	C	1	P	2	NG															
ROSHAN	2	830842	M	3	Y	Y	9	C	1	P	1	NG															
SARADISR	3	830860	F	3	Y	Y	11	C	2	P	1	NG															
B/O SINDH	1	831072	M	3	Y	N	12	C	2	P	1	NG															
VEDAPRIY	2	831073	F	3	Y	Y	13	C	2	P	2	NG															
PRITHVI	3	831074	M	4	Y	Y	14	C	2	P	1	NG															
B/O SHYAI	1	831112	M	5	Y	N	15	C	2	P	3	G	STAPH	R	R	R	R	R	S	S	S	S	S	S			S
SAMUVEL	2	831114	M	4	Y	Y	9	C	2	P	2	NG															
KRITHIKA	3	831120	F	3	Y	Y	8	C	2	P	1	NG															
LILITHA	2	831123	F	3	Y	Y	7	C	2	P	1	NG															
RAKSHITH	1	831124	F	3	Y	Y	9	C	2	P	2	NG															
GOKILA	3	831601	F	3	Y	Y	13	C	2	P	1	NG															
DINESHBA	1	831581	M	4	Y	N	14	C	1	P	1	NG															
NITHISWA	2	824506	M	5	N	N	15	D	1	P	4	G	STAPH	R	R	R	R	S	S	R	S	S	R	S			R
AASHIKA	2	826405	F	3	N	Y	14	C	2	P	2	NG															
DEVIPRIY/	3	832226	F	3	Y	Y	10	C	2	P	1	NG															
RAKESH	1	832197	M	4	Y	N	9	C	2	P	2	NG															
RAJAN	1	832288	M	5	Y	N	17	C	1	P	4	G	EC	R	R	R	S	S	R	R	S	S	R	R	S	S	
B/O SUJAT	2	832422	M	5	N	Y	12	C	1	P	3	G	KL	S	S	S	S	S	S	R	S	S	R	R	S	S	
EPZIBA	3	832705	F	3	Y	Y	14	C	2	P	1	NG															
DHARSHA	1	832721	M	3	Y	N	11	C	2	P	1	NG															
PADMESH	2	832712	M	3	Y	Y	16	C	1	P	1	NG															
SUJI	1	832596	F	3	N	N	11	C	1	P	1	NG															
IBRAHIM	3	832707	M	3	Y	Y	12	C	2	P	2	NG															
HARIPRIY/	2	832474	F	3	Y	Y	13	C	1	P	1	NG															
HEMANTH	1	832500	M	3	Y	N	14	C	2	P	1	NG															
JEEVITHA	3	833201	F	5	N	N	15	C	2	P	4	G	STAPH	R	R	R	R	S	S	R	S	S	R	S			S
SRILAKSHI	2	833548	F	4	Y	N	9	C	1	P	1	NG															
PRATHIKA	2	833380	F	5	N	N	14	C	2	P	4	G	STAPH	R	R	R	R	S	S	S	R	R	S	R			S
FEROZ	3	833970	M	3	N	Y	9	C	2	P	2	NG															
SUBASHRE	1	833448	F	3	Y	N	8	C	2	P	1	NG															
MOHITH	2	833449	M	3	Y	Y	10	C	1	P	1	NG															
MADHU	1	833403	F	3	Y	N	11	C	2	P	1	NG															
GURUDHA	2	833476	M	3	Y	Y	12	D	1	P	2	NG															
BHARATHI	3	833452	F	3	Y	Y	13	C	1	P	1	NG															
ABHIBA	1	833114	F	3	N	N	15	C	2	P	1	NG															
SAIKRISHN	2	833677	M	4	N	Y	16	C	1	P	4	G	STAPH	R	R	R	S	S	S	S	R	R	R	R			S
SUMITHR/	3	833657	F	5	N	N	16	C	2	P	4	G	KL	R	R	R	S	R	R	R	S	R	R	R	S	S	
B/OLATHA	1	833688	M	3	N	N	9	C	1	P	2	NG															
NAVEEN	2	833646	M	4	Y	Y	8	C	2	P	1	NG															
MAITHESH	3	833654	M	3	Y	Y	10	C	2	P	1	NG															
B/O NEEL/	1	833652	F	3	Y	N	9	C	1	P	2	NG															
NITHYA	3	833694	F	3	Y	Y	9	C	1	P	2	NG															
SAIHARISH	1	833629	M	3	N	N	9	C	2	P	1	NG															
JENINA	2	833665	F	3	Y	Y	8	C	2	P	3	NG															
YUVASHRE	3	833909	F	3	Y	Y	7	C	2	P	1	NG															
LOGANAT	1	833928	M	3	Y	N	10	C	2	P	2	NG															
KRISHNAN	2	833937	M	3	Y	Y	11	C	2	P	1	NG															
ABHISHYA	3	833895	F	3	N	Y	12	C	1	P	1	NG															
SAMEER	2	833884	M	4	N	N	14	C	1	P	4	G	STAPH	R	R	R	R	R	S	S	S	R	R	S			S
SUNDARA	1	833929	M	5	N	N	15	C	1	P	4	G	STAPH	R	R	R	R	R	S	R	R	R	R	S			S
DEEPIKA	1	834227	F	4	Y	N	11	C	2	P	3	NG															
DHANAM	3	834229	F	5	Y	Y	16	C	1	P	4	G	STAPH	R	S	S	R	R	S	S	S	S	S	S			S
ALIULLAH	1	834230	M	4	Y	N	9	C	1	P	2	NG															
AVINASH	1	834234	M	3	Y	N	8	C	2	P	2	NG															
SIVAPRAK	2	834240	M	3	Y	N	9	C	2	P	1	NG															
CHELLIAH	3	834244	M	3	Y	Y	7	C	2	P	1	NG															
KAVIN	3	834245	M	5	N	Y	14	C	1	P	4	G	STAPH	R	R	R	S	S	S	R	S	S	R	S			S
RISHIBALA	1	834247	M	5	N	N	15	C	1	P	4	G	STAPH	S	S	S	S	S	S	S	S	S	S	S			S
ABINAV	2	834278	M	4	Y	Y	16	C	2	P	4	G	ENT	R	R	R	S	R	R	R	S	S	R	S	S	S	
LOHITH	3	834396	M	3	Y	Y	13	C	2	P	2	NG															
ASHMITH/	1	834579	F	3	Y	N	11	C	1	P	3	NG															
B/O KALP/	2	834564	F	3	Y	Y	8	C	2	P	2	NG															
JOEL	2	835297	M	5	N	N	14	C	1	P	4	G	STAPH	S	S	S	S	S	S	S	S	S	S	S			S
SIVABALA	3	836020	M	4	N	Y	10	C	1	P	2	NG															
ABDUL RA	1	835994	M	3	Y	N	11	C	2	P	2	NG															
MUKESH	3	835984	M	3	Y	Y	13	C	1	P	1	NG															
DHARUN	1	835978	M	5	N	N	16	C	1	P	4	G	KL	R	R	R	R	S	S	S	S	S	S	S	S	S	
DIVYADH/	2	835995	F	3	Y	Y	18	C	2	P	3	NG															
SRIDAR	2	835982	M	3	Y	Y	11	C	1	P	2	NG															
SANTHOSI	1	835983	M	3	Y	N	12	C	2	P	3	NG															
SHANMUG	3	835992	F	3	Y	Y	16	C	1	P	4	G	STAPH	S	S	S	S	S	S	S	S	S	S	S			S
NITHIN	2	836786	M	3	Y	N	9	C	2	P	2	NG															
RISHIKANT	1	836784	M	3	Y	N	8	C	2	P	3	NG															
STEPHENR	3	836785	M	4	Y	Y	9	C	2	P	1	NG															
KABINATH	2	837312	M	3	Y	Y	10	C	1	P	2	NG															
JEEVASRI	1	837317	F	5	Y	N	11	C	2	P	3	NG															
SARATH	3	837320	M	3	Y	Y	15	C	2	P	2	NG															
JACQUELI	2	837370	F	3	Y	Y	13	C	2	P	1	NG															
IBA	1	838368	F	3	Y	N	12	C	2	P	2	NG															
SANTHOSI	2	838379	M	3	Y	Y	8	C	2	P	2	NG															
MOHAN	1	838380	M	4	N	N	15	C	1	P	4	G	KL	R	R	R	R	R	R	R	S	S	R	R	S	S	
KEERTHAN	3	838382	F	3	Y	Y	11	C	2	P	2	NG															
NIRANJAN	2	838383	M	3	Y	N	9	C	2	P	1	NG															
JEBA	1	838385	F	3	Y	N	8	C	1	P	1	NG															
CHITRA	1	838386	F	5	Y	N	17	D	1	P	4	G	ENT	R	R	R	R	R	R	R	R	R	R	R	R	R	
SANJANA	1	838389	F	5	Y	N	14	C	1	P	3	NG															
JAYAKUM/	2	838390	M	3	Y	Y	15	C	2	P	1	NG															
NAREN	3	838392	M	3	Y	Y	8	C	2	P	2	NG															
JAGADEES	3	838394	M	5	N	N	17	C	2	P	2	G	PS	R	R	R	R	R	R	R	S	R	R	R	S	S	
KARTHI	2	838397	M	4	Y	N	11	C	2	P	2	NG															
SUVETHA	3	838398	F	4	N	N	12	C	1	P	3	G	STAPH	S	S	S	S	S	S	S	S	S	S	S			S
VIMAL	2	838399	M	5	N	N	12	C	2	P	4	G	STAPH	R	S	S	S	S	S	S	S	S	R	S			S
APPU	1	838400	M	5	N	N	14	C	1	P	4	G	STAPH	R	R	R	R	R	S	R	R	R	R	S			S
KARTHIK	3	838411	M	3	Y	Y	8	C	2	P	2	NG															
SAROJA	2	838420	F	4	Y	Y	9	C	2	P	1	NG															
SARANYA	1	838424	F	3	N	N	8	C	2	P	1	NG															
LOGESH	3	838425	F	3	Y	Y	9	C	2	P	2	NG															
VETRIVEL	1	838427	M	5	N	N	14	D	1	P	4	NG															
DARUNESI	2	838429	M	4	N	N	16	D	2	P	3	NG															
JEYACHAN	2	838430	M	4	N	N	14	C	2	P	4	G	KL	R	R	R	S	S	S	S	S	S	R	R	S	S	
VARUN	1	838440	M	5	Y	N	17	C	2	P	3	G	STAPH	R	R	R	S	S	S	S	S	R	R	S			S